Evidence for Two Regions in the Mouse t Complex Controlling Transmission Ratios

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SUMMARY

Four new t haplotypes, tTul through tTu4, are described, three of them derived from the twlHf haplotype and one (tTui) from the twi haplotype. The tTul and tTu4 haplotypes cause taillessness in T/tTul or T/tTu4 heterozygotes, lack the lethality factor, weakly suppress recombination in the T-H-2 interval, and are transmitted to offspring from tTu/ + males at nearly Mendelian ratios. The tTu3 haplotype resembles tTul and tTui except for the fact that the T/tTu3 heterozygotes have normal-length tails. The tTu2 haplotype probably carries the lethal factor of twlHf, suppresses crossing-over in the T-H-2 and tf-H-2 intervals, and displays a slightly subnormal transmission ratio. In the compound heterozygote tTu1/tTu2, the male transmission ratio of the tTu1 chromosome is close to that of the original twlHf haplotype. A similar effect is observed in the tTu3/tTu2 heterozygote. This observation is interpreted as evidence for two regions within the t complex controlling the male transmission ratios. One of the regions is close to the tail-modifying region, the other is close to the lethality factor. Our findings parallel closely those made in the segregation distorter system in Drosophila.

1. INTRODUCTION

The t complex of the mouse is a group of genes affecting tail length, embryonic differentiation, male fertility, segregation of genes in progeny, and the frequency of crossing-over (Bennett, 1975; Klein & Hammerberg, 1977). The complex occupies a segment of chromosome 17 extending from the centromere to at least the tufted locus (tf, affecting hair growth), and perhaps even further to the H-2 system (the major histocompatibility complex or MHC of the mouse, cf. Klein & Hammerberg, 1977). The segment can be divided into three regions, T, A, and L, each concerned with some of the t-syndrome traits (Lyon et al. 1979). The T region is marked by the dominant mutation Brachyury or short tail (T) responsible for the absence of a variable number of terminal tail vertebrae in T/+ heterozygotes.

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Another mutation in this region, *tailless* (*t*), is recessive in combination with the wild allele (*t/+* mice have normal tails) and codominant in combination with the *short-tail* allele (*T/t* mice lack all tail vertebrae). The *A* region controls the transmission of linked genes to the offspring: some mutations in this region are responsible for the transmission of the *t* chromosome from *t—* heterozygous males to more than the expected one-half of the progeny (often in excess of 90%), others change the transmission ratio in favour of the non-*t* chromosome. Mutations in the *L* region result in the death of some or all mutant homozygotes. At least seven mutant alleles have been identified in this region, each responsible for embryonic death at a specific time of gestation and producing characteristic symptoms. Mutations in the *L* region also cause complete or partial sterility of males homozygous for a given *t* mutation (in instances where such animals live) or of males heterozygous for different *t* mutations. Each particular combination of mutant *t* alleles (the *t* haplotype) is held together in a single chromosome by a suppressor of recombination which reduces the frequency of crossing-over in the segment between the *T* and the *H-2* regions from the normal value of about 14% to less than 1%. The nature and position of the crossing-over suppressor are not known.

In this communication we carry the genetic dissection of the *t* complex a step further by demonstrating that the effect on transmission ratios is, in fact, exerted by two separate but interacting regions of chromosome 17.

### 2. MATERIALS AND METHODS

#### (i) Mice

The *T/tw12tf* subline was derived from the *T tf/twl2+* strain maintained at the Sloan-Kettering Institute for Cancer Research in New York (Bennett, 1975). The spontaneous change of the wild allele into *tf* in the *t*-bearing chromosome remains unexplained. However, since the two strains have the same *H-2* haplotype and since, apparently, their *tw12* haplotypes do not differ either, recombination is an unlikely explanation; more probably, the *tufted* phenotype is the result of a mutation at the *tf* locus. The original *tw12* haplotype was extracted from wild mice captured at Oakland, California (Dunn, Bennett & Beasley, 1962). From *tw12/*—homozygous males, the *tw12* chromosome is transmitted to 95% of the progeny, and all *tw12/tw12* homozygotes die at 12 days of gestation (reviewed by Bennett, 1975).

The *tw2* haplotype of the *T tf/tw2* strain came originally from a wild mouse captured in New York (Dunn & Suckling, 1956). The *tw2* chromosome is transmitted by heterozygous males to about 95% of the progeny. Most of the *tw2/tw2* homozygotes die before birth but some live to reach maturity. Crossing-over in the *T-H-2* interval is suppressed by the presence of *tw2* (reviewed by Bennett, 1975).

The B10. Rb7D strain originated from a cross between C57BL/10Sn (abbreviated as B10) and a wild mouse carrying seven pairs of Robertsonian translocations. The hybrids were repeatedly backcrossed to B10 (in odd-numbered backcross
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and B10.D2 (in even-numbered generations) until a congenic line was established carrying only one Robertsonian translocation, \( \text{Rb}(16.17) \) 7Bnr. The metacentric chromosome of the B10.Rb7D strain carries the H-2 haplotype.

(ii) **Serological tests**

The H-2 haplotypes of segregant mice were ascertained by the polyvinylpyrrolidone (PVP) hemagglutination test described elsewhere (Klein, Hauptfeld & Hauptfeld, 1975). Antisera to H-2 antigens were produced as reported previously (Zaleska-Rutczynska & Klein, 1977).

(iii) **Karyotyping**

The segregation of the Robertsonian translocation (a metacentric chromosome) was determined from peripheral blood cell smears prepared by the method of Triman, Davisson & Roderick (1975).

(iv) **Origin of \( t \) recombinants**

In crosses set up for a different purpose, Dr Ellen Hsu, while working at our Institute, obtained four exceptional animals which could best be explained as recombinants in the region occupied by the \( t \) complex (see below). We designate the \( t \) haplotypes carried by these recombinants \( t^{Tu1} \) through \( t^{Tu4} \), where \( Tu \) stands for Tübingen.

The \( t^{Tu1} \) haplotype arose in the cross \(+ t^{w12tf} H-2^{w30}/Rb7^+ H-2^d \times + + + H-2^b/++ + H-2^b\), originally designated to determine the effect of \( t^{w12} \) on crossing-over between the centromere (marked by the Robertsonian translocation) and \( t^{w12} \). The exceptional male had a normal tail and lacked the Rb7 translocation, but carried the H-2\(^d\) haplotype, suggesting that his one chromosome had derived the centrometic portion from the \( t^{w12} \) haplotype and the telomeric portion from the metacentric chromosome. Hence, the crossing-over occurred somewhere between the centromere and the H-2 complex.

The \( t^{Tu2} \) haplotype originated from the cross \( t^{w12tf} H-2^{w30}/T^tf H-2^d \times t^{Tu1} + H-2^d/++ + H-2^b \). The exceptional male was tailless and a \( H-2^{w30}/H-2^d \) heterozygote suggesting that his recombinant haplotype, derived by crossing-over between the \( T \) locus and the H-2 complex, retained the telomeric portion but lost the centromeric portion of the \( t^{w12tf} \) haplotype. Hence the \( t^{Tu2} \) haplotype originated through an event reciprocal to the one that gave rise to the \( t^{Tu1} \) haplotype.

The \( t^{Tu3} \) haplotype originated from the cross \( Rb7^+ + H-2^d/ + t^{w12tf} H-2^{w30} \times + + + H-2^k/++ + H-2^k \). The exceptional animal lacked the metacentric chromosome but carried the \( H-2^d \) haplotype suggesting that it originated by crossing-over between the centromere and H-2.

The \( t^{Tu4} \) haplotype was discovered in an exceptional tailless-tufted female...
produced in the balanced-lethal mating $T t^{w2} + \times T t^{w2} t^{f}$. Further testing revealed that the recombinant haplotype carried the centromeric region of $t^{w2}$ and the telomeric portion of the $T t^{f}$ chromosome (see RESULTS).

3. RESULTS

We analysed the four $t^{Tu}$ haplotypes in a series of crosses designed to test for the individual properties of the $t$ haplotypes: effect on tail length, effect on recombination frequency, viability, and segregation of chromosomes in males.

Table 1. Effect of the $t^{Tu}$ haplotypes on tail-length

| Genotype          | Phenotype |
|-------------------|-----------|
| $T/t^{Tu1}$       | Tailless  |
| $+/t^{Tu1}$       | Normal tail|
| $t^{Tu1}/t^{Tu1}$ | Normal tail|
| $T/t^{Tu2}$       | Lethal    |
| $+/t^{Tu2}$       | Short tail|
| $t^{Tu2}/t^{Tu2}$ | Lethal    |
| $T/t^{Tu3}$       | Normal tail|
| $+/t^{Tu3}$       | Normal tail|
| $t^{Tu3}/t^{Tu3}$ | Not available|
| $T/t^{Tu4}$       | Tailless  |
| $+/t^{Tu4}$       | Normal tail|
| $t^{Tu4}/t^{Tu4}$ | Not available|

(a) Effect on tail length

From the various crosses performed (data not shown) one can deduce the relationship between the genotype and the tail phenotype as shown in Table 1. Two of the four recombinant $t$ haplotypes ($t^{Tu1}$ and $t^{Tu4}$) behave in an orthodox way: they enhance the effect of the Brachyury gene so that the $T/t^{Tu}$ heterozygotes are tailless, and they have no demonstrable effect on the wild allele so that the $+/t^{Tu}$ heterozygotes have normal tails. The other two haplotypes behave differently: the $t^{Tu2}$ haplotype is lethal in combination with $T$ (see below) probably because it itself carries the Brachyury gene (a contention supported by the short-tailedness of the $+/t^{Tu2}$ heterozygotes); the $t^{Tu3}$ suppresses rather than enhances the effect of the Brachyury gene so that the $T/t^{Tu3}$ animals have normal tails.

(b) Effect on viability

The results from crosses designed to test the new $t$ haplotypes for their effect on the viability of $t^{Tu}/t^{Tu}$ homozygotes and $t^{Tu}/t^{w}$ compound heterozygotes are summarized in Table 2. Mice carrying the $t^{Tu1}$ haplotype are viable both as $t^{Tu1}/t^{Tu1}$ homozygotes and $t^{Tu1}/t^{w12} t^{f}$ heterozygotes. The $t^{Tu1}$ haplotype thus appears to have lost the lethality factor of the original $t^{w12} t^{f}$ haplotype. With respect to the $t^{Tu2}$ haplotype, the only viable gene combination of those tested is...
Table 2. Tests for viability of t-recombinant chromosomes in combination with parental t chromosomes

| Progeny | Genotype of mother | Genotype of father | Genotype | Expected* | Observed | χ² |
|---------|-------------------|-------------------|----------|-----------|----------|----|
|         | iTu1 + H-2d / iTu1 + H-2d | tU12 tf H-2w30 / + + H-2k | iTu1 + H-2d / tU12 tf H-2w30 | 18.05 | 14.00 | 18.17 |
|         |                   |                   | iTu1 + H-2d / + + H-2k | 0.95  | 5.00  |     |
|         | iTu1f H-2w30 / + + H-2d | tU12 tf H-2w30 / + + H-2k | iTu1f H-2w30 / tU12 tf H-2w30 | 22.32 | 0.00  |     |
|         |                   |                   | iTu1f H-2w30 / + + H-2k | 1.18  | 6.00  |     |
|         |                   |                   | + + H-2d / tU12 tf H-2w30 | 22.32 | 34.00 | 76.82 |
|         |                   |                   | + + H-2d / + + H-2k | 1.18  | 7.00  |     |
|         | T + H-2b / iTu3 + H-2d | tU12 tf H-2w30 / + + H-2k | T + H-2b / tU12 tf H-2w30 | 3.32  | 2.00  |     |
|         |                   |                   | iTu3 + H-2b / tU12 tf H-2w30 | 3.32  | 3.00  |     |
|         |                   |                   | T + H-2b / + + H-2k | 0.18  | 1.00  | 7.99 |
|         |                   |                   | iTu3 + H-2b / + + H-2k | 0.18  | 1.00  |     |
|         | iTu1f H-2b / + + H-2b | tU2 + H-2w12 / T tf H-2b | + + H-2b / tU2 + H-2w12 | 4.75  | 2.00  |     |
|         |                   |                   | iTu1f H-2b / tU2 + H-2w12 | 4.75  | 5.00  |     |
|         |                   |                   | + + H-2b / T tf H-2b | 0.25  | 1.00  | 16.08 |
|         |                   |                   | iTu1f H-2b / T tf H-2b | 0.25  | 2.00  |     |

* Calculated assuming a t-transmission ratio of 0.95 for both tU12 if and tU2 (Bennett, 1975).
+ / TTu2; no TTu2/TTu2, TTu2/tw12 tf, or T/tTu2 animals could be obtained. The lethality of the T/tTu2 heterozygotes can be explained by the presence of the Brachyury gene in TTu2 but the lethality of the TTu2/tTu2 homozygotes and the TTu2/tw12 tf compound heterozygotes is probably caused by the retention of the tw12 tf lethality factor in the TTu2 haplotype. As for the TTu3 and TTu4 haplotypes, although we have not been able to obtain Ttu/tTu homozygotes, we assume that both haplotypes have lost the tw12 tf lethality factor because both the TTu3/tw12 tf and the TTu4/tw2 heterozygotes are viable.

Table 3. Frequency of crossing-over in the T-H-2 interval in the presence of TTu1, TTu2, TTu3, or TTu4.

| Genotype of parent | Number of progeny | Frequency of crossing-over |
|--------------------|------------------|----------------------------|
| | Parental | Recombinant | | |
| T+H-2x/tTu1+H-2d | 74 | 7 | 0-09 | 1-31 |
| TTu2 tf H-2w30/+ + H-2x +/+ or tf/tf | 216 | 8 | 0-04 | 17-35 |
| T+H-2x/tTu3+H-2d | 36 | 6 | 0-14 | 0-07 |
| T tf H-2x/TTu4 if H-2b +/+ | 31 | 3 | 0-09 | 0-88 |
| ++ H-2x/tTu4 if H-2b T/+ | 29 | 3 | 0-09 | 0-36 |

* Calculated in comparison to the expected 12-9 cM distance between T and H-2 in the absence of t (Klein, 1975).

(c) Effect on genetic recombination in the T-H-2 interval

In non- T chromosomes, the T locus recombines with the H-2 complex with a frequency of 14-7 % in females and 12-9 % in males (Klein, 1975). In heterozygotes carrying the tw12 tf or the tw2 haplotypes, these frequencies are reduced to less than 1 % (Bennett, 1975). Of the four Ttu haplotypes, Ttu1, Ttu3, and Ttu4 either permit normal recombination or only slightly reduce the frequency of crossing-over in the T-H-2 interval; the TTu2 haplotype reduces this frequency to about 4 % (Table 3). Apparently the reduction affects not only the T-tf but also the tf-H-2 interval (Table 4) which is normally between 3-5 and 5-5 cM long (Klein, 1975), and probably occurs also in TTu2/TTu1 and TTu2/TTu3 heterozygotes (Table 4).

(d) Effect on chromosome segregation

In matings involving males heterozygous for the haplotypes tw12 tf and tw2, the mutant chromosomes are transmitted to approximately 95 % of the progeny (Bennett, 1975). In contrast, all four Ttu haplotypes have either normal or slightly lowered transmission ratios of the mutant chromosome when the father is either a +/Ttu or T/tTu heterozygote (Table 5). Normal transmission ratios occur also when the father is a Ttu1/Ttu3 or a Ttu1/Ttu4 heterozygote. But the Ttu1/Ttu2 or Ttu3/Ttu2 males transmit the Ttu1 or Ttu3 chromosomes to some 90 % of their progeny, that is, at a ratio approaching that of the original tw12 tf chromosome.
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Table 4. Frequency of crossing-over in the tf-H-2 interval in the presence of t\textsuperscript{T}u\textsubscript{2}

| Genotype of father | Genotype of mother | Parental | Recombinant | Frequency of crossing-over | $\chi^2$* |
|--------------------|--------------------|----------|-------------|---------------------------|---------|
| $t^{T_u}tfH-2w^{30}/++H-2^x$ | tf/tf | 216 | 2 | 0.009 | 7.65 |
| $t^{T_u}tfH-2w^{30}/t^{T_u}+H-2^d$ | tf/tf | 161 | 0 | 0 | 8.47 |
| $t^{T_u}tfH-2w^{30}/t^{T_u}3+H-2^d$ | tf/tf | 18 | 0 | 0 | 0.95 |

* Calculated in comparison to the expected 5 cM distance between tf-H-2 in the absence of t (Sherman, 1977).

Table 5. Effect of recombinant t haplotypes on chromosome segregation

| Genotype of father | Genotype of mother | Progeny with chromosome 2 | Total progeny tested | $\chi^2$* |
|--------------------|--------------------|--------------------------|----------------------|---------|
| $T^{T_u}H-2^x/t^{T_u}+H-2^d$ | ++/+ | 28 | 45 | 62 | 194 | 2.06 |
| ++/+ | 59 | 47 | 132 | 7.40 |
| ++/+ | 88 | 44 | 216 | 59 |
| ++/+ | 17 | 45 | 36 | 0.86 |
| ++/+ | 20 | 44 | 59 | 5 |
| $H-2x/t^{T_u}4$ | ++/+ | 14 | 45 | 31 | 0.20 |
| $H-2^x/t^{T_u}4/t^{H-2}b$ | T'/H-2d' | 25 | 49 | 51 | 82 |
| $H-2^x/t^{T_u}4/t^{T_u}3$ | T'/H-2d' | 255 | 94 | 269 | 215.92 |
| $H-2^x/t^{T_u}3/t^{H-2}d$ | ++/+ | 17 | 94 | 18 | 14.22 |
| $H-2^x/t^{T_u}4/t^{H-2}b$ | ++/+ | 23 | 51 | 45 | 0.02 |
| $T^{T_u}+H-2^d/t^{T_u}4+H-2^d$ | T'/H-2d' | 11 | 50 | 22 | 0.00 |

* Calculated in comparison to the expected Mendelian values.

4. DISCUSSION

The properties of the four $t^{T_u}$ haplotypes are summarized in Table 6; their postulated mode of origin is depicted in Fig. 1. The fact that in all four $t^{T_u}$ haplotypes, the two most distant markers on the chromosome 17, the centromere or the Brachyury gene and the H-2 complex, have recombined leads us to conclude that the haplotypes arose by crossing-over within the $t$ complex. In three of the haplotypes, $t^{T_u}1$, $t^{T_u}3$ and $t^{T_u}4$, the crossing-over resulted in the loss of the lethality factor present in the original $t^{w12}$ tf and $t^{w2}$ haplotypes; in the fourth haplotype, $t^{T_u}2$, the lethality factor was apparently retained. Since the lethality factors are believed to be located in the vicinity of the tufted gene (Lyon et al. 1979), the crossing-over must have taken place between the centromere and the tf region. In three of the recombinants ($t^{T_u}1$, $t^{T_u}2$ and $t^{T_u}4$), the tail-modifying region, believed to be located at a position homologous to the Brachyury gene, was inherited en bloc so that the crossing-over giving rise to these recombinants, must have occurred between the $T$ and $tf$ loci. In the fourth recombinant, $t^{T_u}3$, the crossing-over might have occurred within the tail-affecting region. This recombinant, unlike most other
Table 6. Properties of $t^{tw12}$, $t^{tw2}$, and their derivatives: A summary.

| Haplotypes | Tail length of $T/t$ mice | Viability of $t^2/t^2$ homozygotes | Recombination $(T\cdot H\cdot 2)$ | Transmission of $t$ |
|------------|---------------------------|-----------------------------------|---------------------------------|------------------|
| $t^{tw12}tf$ | Tailless                  | Lethal                            | Strongly suppressed             | Very high        |
| $t^{tw2}$   | Tailless                  | Semiviable                        | Strongly suppressed             | Very high        |
| $t^{Tu1}$   | Tailless                  | Viable                            | Weakly suppressed               | Normal           |
| $t^{Tu2}$   | Short (?)                 | Lethal                            | Suppressed                      | Subnormal        |
| $t^{Tu3}$   | Normal                    | Viable?                           | Normal                          | Normal           |
| $t^{Tu4}$   | Tailless                  | Viable?                           | Weakly suppressed               | Normal           |
| $t^{Tu1}/t^{Tu2}$ | Normal              | Viable                            | Not tested                      | Very high ($t^{Tu1}$) |
| $t^{Tu3}/t^{Tu2}$ | Normal              | Viable                            | Not tested                      | Very high ($t^{Tu3}$) |
| $t^{Tu1}/t^{Tu3}$ | Normal              | Viable                            | Not tested                      | Normal           |
| $t^{Tu1}/t^{Tu4}$ | Normal              | Viable                            | Not tested                      | Normal           |

Fig. 1. Proposed mode of origin of $t^{Tu1}$, $t^{Tu2}$, $t^{Tu3}$ and $t^{Tu4}$ haplotypes.

The $t^{Tu3}$ haplotype is not the first described that interacts with $T$ to produce normal-tailed animals. Another case is the $h^7$ haplotype described by Lyon & Meredith (1964). The $h^7$ haplotype seems to have retained the lethality and crossing-
over-suppression factors of the \( t^6 \) haplotype, from which it derives; the only regions that have changed in \( t^{th7} \), in comparison with \( t^6 \), appear to be those containing the tail-modifying and the segregation-distortion factors. Lyon & Meredith (1964) postulated that the \( t^{th7} \) haplotype arose from \( t^6 \) by unequal sister-strand crossing-over that led to the duplication of the \( T \)-modifying factor in \( t^{th7} \). It is difficult to apply this interpretation to the \( t^{Tu3} \) haplotype because this haplotype clearly arose by crossing-over between nonsister strands of chromosome 17. However, it is also true that our interpretation of \( t^{Tu3} \) is difficult to apply to \( t^{th7} \). Further analysis will, therefore, be necessary to arrive at a unifying explanation of the tail-affecting region in the \( t \) haplotypes.

The observation that reciprocal \( t \) recombinants, such as \( t^{Tu1} \) and \( t^{Tu2} \), distort segregation ratios more strongly, when combined in a \( t^{Tu1}/t^{Tu2} \) heterozygote, than either of them singly, suggests the existence of complementing segregation-distortion regions in the \( t^{u12} t^f \) haplotype. While the \( t^{Tu1} \), \( t^{Tu2} \) and \( t^{Tu3} \) haplotypes were transmitted to the offspring in slightly subnormal ratios, in the compound heterozygotes \( t^{Tu1}/t^{Tu2} \) and \( t^{Tu3}/t^{Tu2} \), the \( t^{Tu1} \) and \( t^{Tu3} \) chromosomes, respectively, were transmitted to about 90% of the offspring. No such distortion of segregation ratios was observed in the \( t^{Tu1}/t^{Tu3} \) and \( t^{Tu1}/t^{Tu4} \) heterozygotes. We interpret these findings as follows. We postulate that there are at least two loci, \( R \) and \( D \), in the \( t^{u12} t^f \) haplotype affecting segregation of the \( t^{u12} t^f \) chromosome. When occurring together on the same chromosome in a male parent, they cause this chromosome to be transmitted to more than the expected 50% of the offspring. Our recombinants have separated these two loci in such a way that, in the \( t^{Tu1} \), \( t^{Tu3} \) and \( t^{Tu4} \) haplotypes, the mutant \( d \) allele was replaced by the wild + allele (the haplotypes are \( R^+ \)), whereas, in the \( t^{Tu2} \) haplotype, the mutant \( R \) allele was replaced by the wild + allele (this haplotype is + \( D \)). In the \( R^+/++ \) and + \( D/++ \) heterozygous males, both chromosomes are transmitted to the progeny at approximately Mendelian ratios. In contrast, in the \( R^+/+D \) heterozygous males, the \( R^+ \) chromosome manages to be transmitted to more offspring than the + \( D \) chromosome does.

The \( R \) locus is probably in the vicinity of the tail-modifying region; the \( D \) locus is near the lethality factor and hence near the \( t^f \) locus. To give a more precise location of the \( R \) and \( D \) loci is difficult at this time. The \( R \) locus must be to the left of the \( t^{Tu3} \) cross-over position, and if it is true that this position lies in the tail-modifying region, as we have postulated, then the \( R \) locus must either lie in this region or be located between this region and the centromere. Furthermore, since whenever \( R \) is separated from \( D \) in a \( t \) recombinant, \( D \) always appears to go with the lethality factor, \( D \) and the lethality factor are probably close to each other on the chromosome.

The \( R \) and \( D \) genes are probably not restricted to the \( t^{u12} t^f \) and \( t^{u2} \) haplotypes but rather occur in most if not all \( t \) haplotypes. Complementing genes affecting segregation of \( t \) chromosomes have, in fact, been described by Lyon & Mason (1977) who studied haplotypes derived from \( t^6 \). These authors demonstrated that in several instances compound \( t^hz/t^hv \) heterozygous males transmitted one of the \( t^h \)
chromosomes to a higher percentage of offspring than did $t^b/+\) heterozygotes. This finding, too, suggests the interaction of two separate loci or regions in the $t$ complex. The relationship of these loci to the $R$ and $D$ loci described in this communication is not yet clear. There are important differences between the two systems (e.g. the male transmission ratio of the $t^b$ haplotype is only 0.65, most of the complementing haplotypes display a low transmission ratio of about 0.22, and complementation restores normal ratios rather than causing a high ratio of one of the haplotypes involved) indicating that the genetic control of the male transmission ratios may be more complicated than our data suggest. A direct comparison of the $t^{Tu}$ and $t^b$ haplotypes will be necessary to clarify the relationship between the two.

Table 7. Comparison of segregation distorters in the $t$ complex of the mouse and the $Sd$ system of Drosophila

| Mouse Genotype | Example | Transmission ratio of chromosome in 1st position | Drosophila Genotype |
|---------------|---------|-----------------------------------------------|---------------------|
| $RD+/+\) | $t^{u12}/+/+\) | High | $Sd\) $Rsp/++\) |
| $R+/+\) | $t^{u1}/+/\) | Normal | $++/++\) |
| $+D+/+\) | $t^{u2}/+/\) | Normal | $Sd+/+/+\) |
| $R+/+D\) | $t^{u1}/t^{u2}\) | High | $++/Sd\) |
| $R\)D/R\) | $t^{u12}/f/\) | Normal | $Sd\) $Rsp/+\) |

* Not tested.

The control of transmission ratios described here is remarkably similar to that described in Drosophila (for a review see Hartl & Hiraizumi, 1976; see also Table 7). The Drosophila segregation distorter system consists of two closely linked loci straddling the centromere of the second chromosome. One of the loci is called segregation distorter ($Sd$) and the other responder ($Rsp$). The latter behaves formally as a recessive suppressor of abnormal segregation (Hartl, 1977). Recombination between the two loci is suppressed by their association with pericentric inversions and, as in the $t$ complex, some of the mutant alleles are also associated with lethality factors. Our $D$ mutation behaves like the fruit fly $Sd$ factor and our $R$ gene corresponds to the Drosophila $Rsp$ factor. The similarity of the effects of the two systems (Table 7) may be superficial and not necessarily an indication of evolutionary homology. However, it is comforting to know that the $t$ complex is not quite as unique as it once seemed to be.

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