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

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SUMMARY

Four new *t* haplotypes, t^{Tu1} through t^{Tu4}, are described, three of them derived from the $t^{w12}tf$ haplotype and one (t^{Tu4}) from the t^{w2} haplotype. The t^{Tu1} and t^{Tu4} haplotypes cause taillessness in T/t^{Tu1} or T/t^{Tu4} heterozygotes, lack the lethality factor, weakly suppress recombination in the *T–H–2* interval, and are transmitted to offspring from $t^{Tu}/+$ males at nearly Mendelian ratios. The t^{Tu3} haplotype resembles t^{Tu1} and t^{Tu4} except for the fact that the T/t^{Tu3} heterozygotes have normal-length tails. The t^{Tu2} haplotype probably carries the lethal factor of $t^{w12}tf$, suppresses crossing-over in the *T-H-2* and *tf-H-2* intervals, and displays a slightly subnormal transmission ratio. In the compound heterozygote t^{Tu1}/t^{Tu2}, the male transmission ratio of the t^{Tu1} chromosome is close to that of the original $t^{w12}tf$ haplotype. A similar effect is observed in the t^{Tu3}/t^{Tu2} 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 $T/t^{w12}tf$ subline was derived from the $T\ tf/t^{w12}+$ 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 t^{w12} 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 t^{w12} haplotype was extracted from wild mice captured at Oakland, California (Dunn, Bennett & Beasley, 1962). From $t^{w12}/-$ heterozygous males, the t^{w12} chromosome is transmitted to 95 % of the progeny, and all t^{w12}/t^{w12} homozygotes die at 12 days of gestation (reviewed by Bennett, 1975).

The t^{w2} haplotype of the $T\ tf/t^{w2}$ strain came originally from a wild mouse captured in New York (Dunn & Suckling, 1956). The t^{w2} chromosome is transmitted by heterozygous males to about 95 % of the progeny. Most of the t^{w2}/t^{w2} homozygotes die before birth but some live to reach maturity. Crossing-over in the *T-H-2* interval is suppressed by the presence of t^{w2} (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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generations) and B10 . D2 (in even-numbered generations) until a congenic line was established carrying only one Robertsonian translocation, 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 $+t^{w12}tf\ H\text{-}2^{w30}/Rb7+H\text{-}2^{d} \times +++H\text{-}2^{b}/+++H\text{-}2^{b}$, 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 $H\text{-}2^{d}$ 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 $t^{w12}tf\ H\text{-}2^{w30}/T\ tf\ H\text{-}2^{q} \times t^{Tu1}+H\text{-}2^{d}/++H\text{-}2^{b}$. The exceptional male was tailless and a $H\text{-}2^{w30}/H\text{-}2^{d}$ 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 $t^{w12}tf$ 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 $Rb7++H\text{-}2^{d}/+t^{w12}tf\ H\text{-}2^{w30} \times +++H\text{-}2^{k}/+++H\text{-}2^{k}$. The exceptional animal lacked the metacentric chromosome but carried the $H\text{-}2^{d}$ 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

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produced in the balanced-lethal mating $T\ tf/t^{w2}+ \times T\ tf/t^{w2}\ tf$. Further testing revealed that the recombinant haplotype carried the centromeric region of t^{w2} and the telomeric portion of the $T\ tf$ 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 $t^{Tu1}/t^{w12}\ tf$ heterozygotes. The t^{Tu1} haplotype thus appears to have lost the lethality factor of the original $t^{w12}\ tf$ haplotype. With respect to the t^{Tu2} haplotype, the only viable gene combination of those tested is

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Table 2. *Tests for viability of* t*-recombinant chromosomes in combination with parental* t *chromosomes*

Genotype of mother	Genotype of father	Progeny: Genotype	Numbers: Expected*	Numbers: Observed	χ^2
$t^{Tu1}+H\text{-}2^d/t^{Tu1}+H\text{-}2^d$	t^{w12} *tf* $H\text{-}2^{w30}/++H\text{-}2^k$	$t^{Tu1}+H\text{-}2^d/t^{w12}$ *tf* $H\text{-}2^{w30}$	18·05	14·00	18·17
		$t^{Tu1}+H\text{-}2^d/++H\text{-}2^k$	0·95	5·00	
t^{Tu2}*tf* $H\text{-}2^{w30}/++H\text{-}2^d$	t^{w12} *tf* $H\text{-}2^{w30}/++H\text{-}2^k$	t^{Tu2}*tf* $H\text{-}2^{w30}/t^{w12}$ *tf* $H\text{-}2^{w30}$	22·32	0·00	76·82
		t^{Tu2}*tf* $H\text{-}2^{w30}/++H\text{-}2^k$	1·18	6·00	
		$++H\text{-}2^d/t^{w12}$ *tf* $H\text{-}2^{w30}$	22·32	34·00	
		$++H\text{-}2^d/++H\text{-}2^k$	1·18	7·00	
$T+H\text{-}2^b/t^{Tu3}+H\text{-}2^d$	t^{w12} *tf* $H\text{-}2^{w30}/++H\text{-}2^k$	$T+H\text{-}2^b/t^{w12}$ *tf* $H\text{-}2^{w30}$	3·32	2·00	7·99
		$t^{Tu3}+H\text{-}2^d/t^{w12}$ *tf* $H\text{-}2^{w30}$	3·32	3·00	
		$T+H\text{-}2^b/++H\text{-}2^k$	0·18	1·00	
		$t^{Tu3}+H\text{-}2^d/++H\text{-}2^k$	0·18	1·00	
t^{Tu4}*tf* $H\text{-}2^b/++H\text{-}2^q$	$t^{w2}+H\text{-}2^{w29}/T$ *tf* $H\text{-}2^b$	$++H\text{-}2^q/t^{w2}+H\text{-}2^{w29}$	4·75	2·00	16·08
		t^{Tu4}*tf* $H\text{-}2^b/t^{w2}+H\text{-}2^{w29}$	4·75	5·00	
		$++H\text{-}2^q/T$ *tf* $H\text{-}2^b$	0·25	1·00	
		t^{Tu4}*tf* $H\text{-}2^b/T$ *tf* $H\text{-}2^b$	0·25	2·00	

* Calculated assuming a *t*-transmission ratio of 0·95 for both t^{w12} *tf* and t^{w2} (Bennett, 1975).

$+/t^{Tu2}$; no t^{Tu2}/t^{Tu2}, t^{Tu2}/t^{w12} *tf*, or T/t^{Tu2} animals could be obtained. The lethality of the T/t^{Tu2} heterozygotes can be explained by the presence of the *Brachyury* gene in t^{Tu2} but the lethality of the t^{Tu2}/t^{Tu2} homozygotes and the t^{Tu2}/t^{w12} *tf* compound heterozygotes is probably caused by the retention of the t^{w12} *tf* lethality factor in the t^{Tu2} haplotype. As for the t^{Tu3} and t^{Tu4} haplotypes, although we have not been able to obtain t^{Tu}/t^{Tu} homozygotes, we assume that both haplotypes have lost the t^{w12} *tf* lethality factor because both the t^{Tu3}/t^{w12} *tf* and the t^{Tu4}/t^{w2} heterozygotes are viable.

Table 3. *Frequency of crossing-over in the* T-H-2 *interval in the presence of* t^{Tu1}, t^{Tu2}, t^{Tu3}, *or* t^{Tu4}.

Genotype of parent		Number of progeny			
Male	Female	Parental	Recombinant	Frequency of crossing-over	χ^{2*}
$T+H\text{-}2^x/t^{Tu1}+H\text{-}2^d$	$+/+$	74	7	0·09	1·31
t^{Tu2} *tf* $H\text{-}2^{w30}/++H\text{-}2^x$	$+/+$ or *tf/tf*	216	8	0·04	17·35
$T+H\text{-}2^x/t^{Tu3}+H\text{-}2^d$	$+/+$	36	6	0·14	0·07
T *tf* $H\text{-}2^x/t^{Tu4}$ *tf* $H\text{-}2^b$	$+/+$	31	3	0·09	0·88
$++H\text{-}2^x/t^{Tu4}$ *tf* $H\text{-}2^b$	$T/+$	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 t^{w12} *tf* or the t^{w2} haplotypes, these frequencies are reduced to less than 1 % (Bennett, 1975). Of the four t^{Tu} haplotypes, t^{Tu1}, t^{Tu3}, and t^{Tu4} either permit normal recombination or only slightly reduce the frequency of crossing-over in the *T-H-2* interval; the t^{Tu2} 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 t^{Tu2}/t^{Tu1} and t^{Tu2}/t^{Tu3} heterozygotes (Table 4).

(*d*) *Effect on chromosome segregation*

In matings involving males heterozygous for the haplotypes t^{w12} *tf* and t^{w2}, the mutant chromosomes are transmitted to approximately 95 % of the progeny (Bennett, 1975). In contrast, all four t^{Tu} haplotypes have either normal or slightly lowered transmission ratios of the mutant chromosome when the father is either a $+/t^{Tu}$ or T/t^{Tu} heterozygote (Table 5). Normal transmission ratios occur also when the father is a t^{Tu1}/t^{Tu3} or a t^{Tu1}/t^{Tu4} heterozygote. But the t^{Tu1}/t^{Tu2} or t^{Tu3}/t^{Tu2} males transmit the t^{Tu1} or t^{Tu3} chromosomes to some 90 % of their progeny, that is, at a ratio approaching that of the original t^{w12} *tf* chromosome.

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Table 4. *Frequency of crossing-over in the* tf-H-2 *interval in the presence of* t^{Tu2}

Genotype of father	Genotype of mother	Number of progeny: Parental	Number of progeny: Recombinant	Frequency of crossing-over	χ^{2*}
t^{Tu2} *tf* $H\text{-}2^{w30}/++H\text{-}2^{x}$	*tf/tf*	216	2	0·009	7·65
t^{Tu2} *tf* $H\text{-}2^{w30}/t^{Tu1}+H\text{-}2^{d}$	*tf/tf*	161	0	0	8·47
t^{Tu2} *tf* $H\text{-}2^{w30}/t^{Tu3}+H\text{-}2^{d}$	*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 Chromosome 1/Chromosome 2	Genotype of mother	Progeny with chromosome 2: No. mice	Progeny with chromosome 2: %	Total progeny tested	χ^{2*}
T tf $H\text{-}2^{x}/t^{Tu1}+H\text{-}2^{d}$	+/+	28 } 87	45 } 45	62 } 194	2·06
$++H\text{-}2^{q}/t^{Tu1}+H\text{-}2^{d}$	+/+	59 }	45 }	132 }	
$++H\text{-}2^{x}/t^{Tu2}$ *tf* $H\text{-}2^{w30}$	+/+	88	41	216	7·40
$T+H\text{-}2^{b}/t^{Tu3}+H\text{-}2^{d}$	+/+	17 } 43	47 } 45	36 } 95	0·86
$++H\text{-}2^{x}/t^{Tu3}+H\text{-}2^{d}$	+/+	26 }	44 }	59 }	
T tf $H\text{-}2^{d}/t^{Tu4}$ *tf* $H\text{-}2^{b}$	+/+	14 } 39	45 } 48	31 } 82	0·20
$++H\text{-}2^{x}/t^{Tu4}$ *tf* $H\text{-}2^{b}$	*T tf* $H\text{-}2^{d}/++H\text{-}2^{x}$	25 }	49 }	51 }	
t^{Tu2} *tf* $H\text{-}2^{w30}/t^{Tu1}+H\text{-}2^{d}$	+/+	255	94	269	215·92
t^{Tu2} *tf* $H\text{-}2^{w30}/t^{Tu3}+H\text{-}2^{d}$	+/+	17	94	18	14·22
$t^{Tu1}+H\text{-}2^{d}/t^{Tu4}$ *tf* $H\text{-}2^{b}$	+/+	23	51	45	0·02
$t^{Tu1}+H\text{-}2^{d}/t^{Tu3}+H\text{-}2^{d}$	$T+H\text{-}2^{b}/++H\text{-}2^{s}$	11	50	22	0·00

* Calculated in comparison to the expected Mendelian values.

4. DISCUSSION

The properties of the four t^{Tu} haplotypes are summarized in Table 6; their postulated mode of origin is depicted in Fig. 1. The fact that in all four t^{Tu} 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^{Tu1}, t^{Tu3} and t^{Tu4}, 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^{Tu2}, 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^{Tu1}, t^{Tu2} and t^{Tu4}), 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^{Tu3}, the crossing-over might have occurred *within* the tail-affecting region. This recombinant, unlike most other

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Table 6. *Properties of* t^{w12} tf, t^{w2} *and their derivatives: A summary.*

t Haplotypes	Tail length of *T/t* mice	Viability of t^x/t^x homozygotes	Recombination (*T-H-2*)	Transmission of *t*
t^{w12} *tf*	Tailless	Lethal	Strongly suppressed	Very high
t^{w2}	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}	Tailless	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

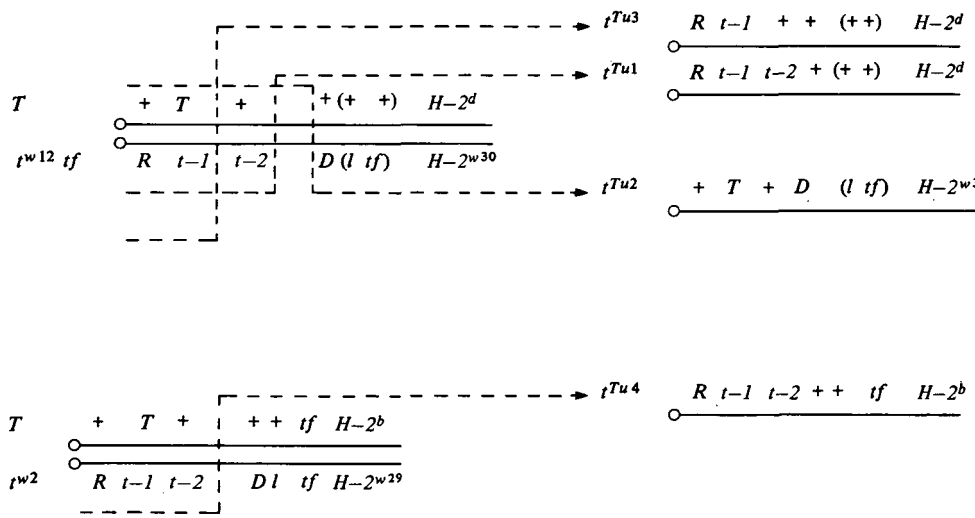

Fig. 1. Proposed mode of origin of t^{Tu1}, t^{Tu2}, t^{Tu3} and t^{Tu4} haplotypes.

known *t* haplotypes, does not enhance the effect of the *Brachyury* gene to produce the tailless phenotype; instead, the T/t^{Tu3} animals have normal tails. One possible way in which the t^{Tu3} haplotype might have arisen is depicted in Fig. 1. Here, we postulate that the tail-modifying region contains at least two genetic elements, *t-1* and *t-2*, one of which is homologous to the *Brachyury* gene. When occurring together in a *cis* configuration the two elements interact with *T* on the homologous chromosome to produce the tailless phenotype; when one of the *t* elements is replaced by a wild allele, as might have happened in t^{Tu3}, the interaction with *T* leads to a normal-tail phenotype.

The t^{Tu3} haplotype is not the first described that interacts with *T* to produce normal-tailed animals. Another case is the t^{h7} haplotype described by Lyon & Meredith (1964). The t^{h7} haplotype seems to have retained the lethality and crossing-

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over-suppression factors of the t^6 haplotype, from which it derives; the only regions that have changed in t^{h7}, 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^{h7} haplotype arose from t^6 by unequal sister-strand crossing-over that led to the duplication of the *T*-modifying factor in t^{h7}. 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^{h7}. 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 segration-distortion regions in the t^{w12} *tf* 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^{w12} *tf* haplotype affecting segregation of the t^{w12} *tf* 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 *tf* 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^{w12} *tf* and t^{w2} 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^{hx}/t^{hy} heterozygous males transmitted one of the t^h

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chromosomes to a higher percentage of offspring than did $t^h/+$ 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^6 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^h 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		Transmission ratio of chromosome in 1st position	*Drosophila*
Genotype	Example		Genotype
RD/++	t^{w12} *tf*/++	High	*Sd Rsp*/++
R+/++	t^{Tu1}/+	Normal	+*Rsp*/++
+*D*/++	t^{Tu2}/+	Normal	*Sd*+/++
R+/+*D*	t^{Tu1}/t^{Tu2}	High	+*Rsp*/*Sd*+
R D/*R*+	t^{w12} *tf*/t^{Tu1}*	Normal	*Sd Rsp*/+*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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