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Absence of detectable gametic disequilibrium between the *t*-complex and linked allozyme-encoding loci in house mice

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To determine the extent of gametic disequilibrium between loci linked to the *t*-complex in house mice, alleles of four allozyme-encoding loci associated with eleven *t*-complexes recently found in wild mice and sixteen *t*-complexes maintained in laboratory colonies were identified. The allozyme-encoding loci included in the survey were complement component-3, kidney catalase, glyoxalase-1 and phosphoglycerate kinase-B. In contrast to published surveys showing strong disequilibrium between the *H-2* complex, *t*-complex protein-1 and the *t*-complex, disequilibrium between the *t*-complex and linked allozyme-encoding loci was not detected. This result is discussed in terms of several hypotheses concerning the structure of mouse populations and the mechanisms maintaining gametic disequilibrium between the *H-2* complex, *t*-complex protein-1 and the *t*-complex.

1. INTRODUCTION

The *t*-complex, which is located on chromosome 17, affects embryonic development, male fertility, meiotic recombination, transmission ratio in heterozygous males, and gametic equilibrium (for reviews of the genetics and developmental biology of the *t*-complex see Bennett (1975), Klein & Hammerberg (1977), and Lyon (1981)). The gametic disequilibrium associated with the *t*-complex is unusual in that three of the nine known examples of disequilibrium in wild house mice involve the *t*-complex. (The linkage map of the relevant loci is given in Fig. 1.) The first example involves the *t* and *H-2* complexes, where only five different *H-2* haplotypes are associated with the eighteen *t*-complexes studied (Hammerberg & Klein, 1975; Hammerberg *et al.* 1976; Hauptfeld, Hammerberg & Klein, 1976; Levinson & McDevitt, 1976; see also Table 1*b*). By contrast, more than one hundred different *H-2* haplotypes have been found in wild mice that do not have a *t*-complex (Duncan, Wakeland & Klein 1979; Nadeau *et al.* 1981). Disequilibrium has also been found between the *t*-complex and *t*-complex protein-1 (*Tcp-1*); all chromosomes bearing an intact *t*-complex have the $Tcp\text{-}1^a$ allele, while all chromosomes that do not have a *t*-complex have the $Tcp\text{-}1^b$ allele (Silver, White & Artzt, 1980). Both of these examples represent complete disequilibrium, because certain alleles or haplotypes have been found only in association with the *t*-complex. The third example involves the t^{w5}-complex and the phosphoglycerate kinase-B allele $Pgk\text{-}2^c$ (Rudolph & VandeBerg, 1981). In contrast to the complete

disequilibrium found between certain *H-2* haplotypes, the *Tcp-1*^{a} allele and the *t*-complex, disequilibrium between *Pgk-2*^{c} and the t^{w5}-complex was not complete. These three disequilibria are believed to be maintained by recombination suppression (Hammerberg & Klein, 1975*a*, *b*), by functional interactions between the loci involved (Snell, 1968; Rudolph & VandeBerg, 1981), or both.

Despite these three examples, disequilibrium between the *t*-complex and linked loci remains inadequately characterized. For example, the only survey of disequilibrium in which some of the allozyme-encoding loci linked to the *t*-complex (Fig. 1) were studied was that by Rudolph & VandeBerg (1982) which included one *t*-complex (t^{w5}) and two allozyme-encoding loci (*Ce-2* and *Pgk-2*). The purpose of the present survey was to extend these analyses of disequilibrium to include (*a*) the loci complement component-3 (*C-3*), kidney catalase-2 (*Ce-2*), glyoxalase-1 (*Glo-1*) and *Pgk-2*, and (*b*) eleven *t*-complexes recently found in wild mice and sixteen *t*-complexes maintained in laboratory colonies for many years.

2. MATERIALS AND METHODS

(*i*) t-*complexes*

The first of two kinds of *t*-complexes included in the survey were those recently found in wild mice. Mice carrying a *t*-complex were identified by crossing wild males to females heterozygous for the brachyury mutation (*T*/+). (Wild females were not included in the survey because they do not usually breed successfully in laboratory colonies.) Such crosses yield tailless (*T*/*t*) progeny only if the wild-derived male carried a *t*-complex. [The relations between phenotype and genotype are the following: normal tail, viable – +/+, +/*t*; short tail, viable – *T*/+; tailless, viable – *T*/*t*; and embryonic lethal – *t*/*t*, *T*/*T*.] Eleven of the more than one hundred males tested sired tailless (*T*/*t*) progeny and therefore carried a *t*-complex (J. H. Nadeau, unpublished observations). The eleven males and their respective *t*-complexes were: BNK 265 (t^{Tuw1}), BNK 266 (t^{Tuw2}), BNK 280 (t^{Tuw3}), BRU 377 (t^{Tuw5}), BRU 382 (t^{Tuw6}), CRO 435 (t^{Tuw7}), CRO 437 (t^{Tuw8}), CRO 447 (t^{Tuw9}), MOY 331 (t^{Tuw14}), MOY 336 (t^{Tuw15}) and MSW 251 (t^{Tuw20}) (Table 1*a*). A description of the origins of these *t*-complexes and their associated *H-2* haplotypes is given by Sturm *et al.* (1982).

The other *t*-complexes included were sixteen of those that have been maintained as balanced lethal lines in laboratory colonies. These were the t^{0}-, t^{6}-, t^{w18}, t^{12}-, t^{w32}-, t^{w1}-, t^{w12}-, t^{w71}-, t^{w75}-, t^{w5}-, t^{w94}-, t^{w73}-, $t^{wPa\text{-}1}$- and $t^{Lub\text{-}1}$-complexes. In addition, mice homozygous for the t^{w2}- and t^{w8}-complexes were included. Unlike most *t*-complex homozygotes, t^{w2}/t^{w2} and t^{w8}/t^{w8} homozygotes are viable but male sterile (Dunn & Suckling, 1956). Reviews of the origins of these *t*-complexes can be found in Hammerberg *et al.* (1976) and Klein & Hammerberg (1977).

(ii) *Linkage phase*

Because many of the mice included in the survey were homozygous for most of the allozyme-encoding loci studied, the allele associated with the *t*-complex was obvious. For example, because *Glo-1* was homozygous (*Glo-1*^{a}/*Glo-1*^{a}) in BNK

265(t^{Tuw1}), *Glo-1*^{a} must be associated with the t^{Tuw1}-complex (Table 1*a*). To determine the linkage phase in heterozygous mice, chromosomes bearing a *t*-complex were placed in combination with genetically defined wild-type chromosomes. (Chromosomes with a *t*-complex are hereafter called *t*-bearing chromosomes, while chromosomes lacking a *t*-complex are hereafter called wild-type chromosomes.) The first of two ways in which this combination of a *t*-bearing chromosome and a wild-type chromosome was achieved involved congenic mice in which the *t*-complex was genetically transferred to the host strains C3H/DiSn (Levinson & McDevitt, 1976) or C57BL/10J (J. Klein, personal communication). (A congenic strain is one in which a chromosomal segment from one strain is genetically transferred into the genome of another strain by repeated backcrossing and selection.) The *t*-complexes made congenic included the t^0-, t^6-, t^{12}-, t^{w32}-, t^{w12}-, t^{w71}-, t^{w75}- and t^{w5}-complexes. Linkage phase between the *t*-complex and alleles of linked loci was deduced by comparing the allozyme phenotype of mice with a *t*-complex to the phenotype of related mice lacking a *t*-complex. For example, a comparison between a tailless C3H/DiSn male (T/t) that is heterozygous PGK-2BC and a C3H/DiSn male with a short tail ($T/+$) that is homozygous PGK-2B indicates that *Pgk-2*^{c} must be associated with the *t*-complex in the tailless mouse.

The second way in which a combination of a *t*-bearing and a wild-type chromosome was achieved involved F_1 mice produced by crossing T/t^x segregating inbred mice to inbred mice such as SM/J, where *x* denotes the *t*-complex involved. These F_1 mice included the t^0-, t^6-, t^{w18}-, t^{w32}-, t^{w5}-, t^{w73}- and t^{w94}-complexes. Phenotypic comparisons were used as described above to determine linkage phase.

In addition, mice homozygous for the t^{w2}- and t^{w8}-complexes were included in the survey. Because animals with these two *t*-complexes were homozygous for every marker studied, linkage phase was obvious and outcrosses were not necessary.

At least two mice from each line were typed for the products of each allozyme-encoding locus. Linkage phase in a few cases remained undefined because of technical difficulties.

(iii) *Electrophoresis*

Electrophoretic and staining methods described by Nadeau *et al.* (1982) were used to type the allozymes C-3 and PGK-2; electrophoretic methods described by E. M. Eicher (personal communication) were used to type the allozymes CE-2 and GLO-1. Loci with co-dominant alleles, *C-3*, *Glo-1* and *Pgk-2*, were tested in wild, congenic and F_1 mice. *Ce-2* was tested only in C3H. t^x mice and mice homozygous for the t^{w2}- or t^{w8}-complexes because *Ce-2*^{b}, which is present in C3H/DiSn, is a recessive allele; other mice in which *t*-complexes are maintained have the dominant allele *Ce-2*^{a}. Polymorphisms of these four loci in natural populations of mice have been described (Rudolph & VandeBerg, 1981; Nadeau, Collins & Klein, 1982; J. Britton-Davidian & J. H. Nadeau, in preparation).

Table 1. *Alleles of loci linked to the t-complex*

(Loci are listed from left to right in increasing distance from the centromere of a wild-type chromosome. '.' indicates 'not done because of technical difficulties or unavailability of appropriate mice'; (*xy*) indicates that linkage phase was not determined, and *x*,*y* that chromosomes bearing this *t*-complex have either of the alleles listed, where *x* and *y* denote the alleles present.)

t-complexes found in wild mice	Complementation group	*Tcp-1**	*Glo-1*	*H-2*†	*Ce-2*	*Pgk-2*	*C-3*	Origin
T^{Tuw1}	.	.	a	w36	a	a	c	Wendelsheim, W. Germany
t^{Tuw2}	.	.	a	w36	b	a	c	Wendelsheim, W. Germany
t^{Tuw3}	.	.	a	w36	(ab)	.	c	Wendelsheim, W. Germany
t^{Tuw5}	.	.	a	w36	a	c	c	Brno, Czechoslovakia
t^{Tuw6}	.	.	a	w36	.	b	c	Brno, Czechoslovakia
t^{Tuw7}	.	.	a	w37	a	a	(bc)	Nahya, Giza Governate, Egypt
t^{Tuw8}	.	.	a	w37	a	a	(bd)	Nahya, Giza Governate, Egypt
t^{Tuw9}	.	.	a	w37	b	a	(bc)	Nahya, Giza Governate, Egypt
t^{Tuw14}	.	.	a	w30	b	a	c	Moya, Spain
t^{Tuw15}	.	.	a	w30	a	a	c	Moya, Spain
t^{Tuw20}	.	.	a	w38	a	b	c	Ryazan, U.S.S.R.
t-complexes maintained in laboratory mice	Complementation group	*Tcp-1**	*Glo-1*	*H-2*†	*Ce-2*	*Pgk-2*	*C-3*	Origin
t^{0}	t^{0}	a	.	w29	b	c	b,c	Paris
t^{6}	t^{0}	a	a	w30	a	b,c	b	Edinburgh
t^{w18}	t^{4}	a	.	.	b	a	b	Storrs, Connecticut
t^{12}	t^{12}	a	a	w28	b	b,c	b	Paris
t^{w32}	t^{12}	a	a	w28	a	b,c	b	Clinton, Montana
t^{w1}	t^{w1}	a	a	w30	b	c	b	New York or Philadelphia
t^{w12}	t^{w1}	a	a	w30	a,b	b,c	b,c	California
t^{w71}	t^{w1}	a	a	w30	a,b	c	b	South Jutland, Denmark
t^{w75}	t^{w1} and t^{w75}	a	a	w31	a	c	b	Jena, E. Germany
t^{w5}	t^{w5}	a	a	w31	a,b	c	b	New York
t^{w94}	t^{w5}	a	a	w31	a	b	c	—
t^{w73}	t^{w73}	a	a	w32	a	b,c	b,c	South Jutland, Denmark
$t^{wPa\text{-}1}$	t^{wPa}	a	.	.	.	a	b,c	Villeneuve-sur-Lot, France
$t^{Lub\text{-}1}$	.	a	a	.	a	a	b,e	Alpie Orobie, Italy
t^{w2}	t^{w2}	a	a	w29	a,b	c	b	New York or Philadelphia
t^{w8}	t^{w2}	a	a	w29	a,b	a	b	Rumford, Virginia

* Data are from Silver *et al.* (1980).

† Data are from Hammerberg & Klein (1975*a*); Hammerberg *et al.* (1976); Hauptfeld *et al.* (1976); Levinson & McDevitt (1976). Nomenclature of Sturm *et al.* (1982) was used. Recent molecular studies (Silver, 1982; Shin *et al.* 1982) support the serological analyses, with the exception that differences were detected between the t^{w5}- and t^{w75}-complexes, both of which share the $H\text{-}2^{w31}$ haplotypes.

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(iv) *Data analysis*

Data for each locus were examined for one of four patterns of disequilibrium. The first pattern was one in which a particular allele was found only in association with *t*-complexes and not in association with wild-type chromosomes; an example is *Tcp-1*^{a} (Silver *et al.*, 1980; see also Table 1*b*). The second pattern was one in which particular alleles are found only in association with *t*-complexes belonging to the same complementation group; an example is *H-2* (Hammerberg & Klein, 1975*a*; Hammerberg *et al.*, 1976; Hauptfeld *et al.* 1976; Levinson & McDevitt, 1976; see also Table 1*b*). The third pattern was one in which a statistical association was detected; an example is *Pgk-2* (Rudolph & VandeBerg, 1981). The fourth pattern was one in which no association was detected. The first two patterns were regarded as evidence for complete disequilibrium, while the third was regarded as evidence for incomplete disequilibrium. In general, very large sample sizes are needed to detect statistical associations indicative of gametic disequilibrium (Brown, 1975). As a result, the present survey could reliably detect the first, second and fourth patterns only.

3. RESULTS

(i) t-*complexes in wild mice*

Among the eleven *t*-bearing chromosomes recently found in wild mice, *C-3*, *Ce-2* and *Pgk-2* were polymorphic while *Glo-1* was monomorphic (Table 1*a*). *C-3*^{c} was the only *C-3* allele found among the eight chromosomes in which linkage phase was determined; linkage phase was not determined in mice with the t^{Tuw7}-, t^{Tuw8}- or t^{Tuw9}-complexes. t^{Tuw8} was the only *t*-complex in which an association with *C-3*^{c} could be excluded. *Ce-2*^{a} was associated with a *t*-complex six times and *Ce-2*^{b} three times; *Ce-2* was not typed in the mouse with the t^{Tuw6}-complex and linkage phase was not determined in the mouse with the t^{Tuw3}-complex. *Pgk-2*^{a} was associated with a *t*-complex seven times, *Pgk-2*^{b} twice and *Pgk-2*^{c} one time; *Pgk-2* was not typed in the mouse with the t^{Tuw3}-complex. Monomorphism of *Glo-1* among these eleven chromosomes was not unexpected because only one *Glo-1* allele has been found in natural populations of house mice (Nadeau *et al.* 1982; J. Britton-Davidian & J. H. Nadeau, in preparation).

Complete disequilibrium between *Ce-2* and *Pgk-2* alleles and *H-2* haplotypes was not detected (Table 1*a*). In most instances, chromosomes sharing similar *H-2* haplotypes were associated with two or more alleles of *Ce-2* and of *Pgk-2*. For example, while chromosomes bearing the t^{Tuw1}- and t^{Tuw2}-complexes shared the *H-2*^{w36} haplotype, *Ce-2*^{a} was associated with the former, *Ce-2*^{b} with the latter. The only exceptions involved *Pgk-2*; *Pgk-2*^{a} was the only *Pgk-2* allele associated with *H-2*^{w30} and with *H-2*^{w37}. Nevertheless, there did not appear to be strong associations between alleles of *Ce-2* and *Pgk-2* and *H-2* haplotypes, or between alleles of these loci and the *t*-complex. *C-3* may be an exception to the pattern observed for *Ce-2* and *Pgk-2* because eight, and perhaps ten, of these eleven *t*-complexes were associated with *C-3*^{c}.

For determining whether there was a statistical association between the

t-complexes and alleles of linked loci, gene-frequency data from an extensive survey of the polymorphisms of *C-3*, *Ce-2*, *Glo-1* and *Pgk-2* in natural populations of house mice were used for calculating the expected gene frequencies among the *t*-bearing chromosomes found in wild mice. These expected frequencies were then compared with the observed frequencies. Summaries of the frequencies of alleles involving *Glo-1*, *Ce-2*, *Pgk-2* and *C-3* in wild mice and their expected frequencies among chromosomes bearing a *t*-complex are given in Table 2 (section pertaining

Table 2. *Comparison of the observed and expected representation of alleles of loci linked to* t*-complexes in wild and laboratory mice**

Locus...	Glo-1		Ce-2		Pgk-2			C-3		
Allele...	Glo-1^a	Glo-1^b	Ce-2^a	Ce-2^b	Pgk-2^a	Pgk-2^b	Pgk-2^c	C-3^b	C-3^c	C-3^d, C-3^g
Allele frequency in natural populations	1·00	0	0·821	0·179	0·558	0·367	0·075	0·360	0·554	0·086
t-complexes in wild mice										
Observed number	11	0	6	3	7	2	1	0	8	—
Expected number	11	0	7·4	1·6	5·6	3·7	0·7	2·9	5·1	0
t-complexes in laboratory mice										
Observed number	10	0	3	9	4	0	11	11	3	1
Expected number	10	0	9·9	2·1	8·4	5·5	1·1	5·4	8·3	1·3

* Expected numbers were obtained by calculating the product of the allele frequency in natural populations and the sample size for each locus. The sample size is equal to the sum of the observed number for each locus, i.e. for Ce-2 sample size is equal to 9 (= 6+3). Data for the allele frequencies in wild mice are from Nadeau *et al.* (1982) and from J. Britton-Davidian & J. H. Nadeau (in preparation). Allele frequencies for Glo-1, Ce-2, Pgk-2 and C-3 were based on samples of 370, 420, 120 and 396 wild mice, respectively. Chromosomes in which linkage phase was ambiguous, i.e. (*xy*) or *x*,*y*, were not included.

to *t*-complexes in wild mice). Although sample sizes were too small to justify statistical analyses, the agreement between expectation and observation was reasonably good. For example, seven *Pgk-2^a*, two *Pgk-2^b* and one *Pgk-2^c* alleles were observed and 5·6, 3·7 and 0·7 were expected, respectively. A possible exception, which was noted above, involved *C-3*, where the *C-3^c* allele may have been represented too often given its frequency in wild mice. In general, alleles associated with these *t*-complexes appear to be random samples of the alleles found in wild mice. If there is disequilibrium involving these loci and the *t*-complex, its magnitude is considerably less than that between the *H-2* complex, *Tcp-1* and the *t*-complex (cf. Hammerberg & Klein, 1975*a*; Hammerberg *et al.* 1976; Hauptfeld *et al.* 1976; Levinson & McDevitt, 1976; Silver *et al.* 1980).

(ii) t-*complexes in laboratory mice*

Among chromosomes bearing the sixteen *t*-complexes maintained in laboratory mice, *Glo-1* was monomorphic and all other loci were polymorphic (Table 1*b*). The interpretation of these data was complicated, however, by the observation that many loci were segregating within the lines used to maintain these *t*-complexes. For example, chromosomes bearing the t^0-complex had either the *C-3*^{b} or the *C-3*^{c} allele. Segregation of one or more loci was observed in each line except those with the t^{w18}-, t^{w1}-, t^{w75}- or t^{w94}-complexes. It is likely that had more mice from each line been tested, the incidence of segregating loci both within and among lines would have been higher. Segregation within lines is consistent with the observed recombination between each of these allozyme-encoding loci and the t^6-complex, and presumably with other *t*-complexes in mice maintained as segregating inbred lines (J. H. Nadeau, in preparation). In addition, irregularities in such a breeding system can significantly delay fixation of alternative alleles (Wright, 1921; Fisher, 1949; Green & Doolittle, 1963).

The frequencies of alleles of three of the four loci (excluding *Glo-1* which was monomorphic) differed considerably between *t*-bearing chromosomes found in wild mice and those maintained in laboratory mice (Table 2; for each locus compare the *observed* number of alleles represented among *t*-complexes in wild mice and *t*-complexes in laboratory mice). For example, *C-3*^{b} was relatively uncommon among *t*-bearing chromosomes found in wild mice but was very common among *t*-bearing chromosomes maintained in laboratory mice. These differences probably reflect acquisition of alleles from the wild-type chromosomes with which *t*-complexes have been maintained in laboratory colonies. Thus, recombination between the allozyme-encoding loci and the *t*-complex has probably eliminated any gametic disequilibrium among *t*-bearing chromosomes maintained in laboratory colonies.

4. DISCUSSION

A survey of the allozyme-encoding alleles associated with the *t*-complex in both wild and laboratory mice revealed no evidence for gametic disequilibrium. These data are in striking contrast to the strong disequilibrium found between the *t*-complex, *Tcp-1* (Silver *et al.* 1980) and the *H-2* complex (Hammerberg & Klein, 1975*a*; Hammerberg *et al.* 1976; Hauptfeld *et al.* 1976; Levinson & McDevitt, 1976).

The apparent absence of disequilibrium between the *t*-complex and linked allozyme-encoding loci provides additional evidence that mouse populations are often not small or highly structured. Although chromosomes obtained from a single population were invariably associated with similar *H-2* haplotypes, these chromosomes were often associated with different combinations of alleles of linked allozyme-encoding loci (Table 1*a*). For example, BNK 265 (t^{Tuw1}) and BNK 266 (t^{Tuw2}) were trapped in the same room of a poultry farm in Wendelsheim, West Germany, during a two-day period in November 1978, yet the former had the *Ce-2*^{a} allele, the latter *Ce-2*^{b} (Table 1*a*). Similar differences were found among chromosomes obtained from three localities in which two or more *t*-complexes were

found (Table 1*a*). It was expected that *t*-bearing chromosomes from a single locality would be related by descent and would therefore show considerable disequilibrium. The frequent occurrence of *t*-bearing chromosomes with different combinations of alleles of linked loci was therefore unexpected, but is consistent with the large numbers of unique *H-2* haplotypes found in mice lacking a *t*-complex and obtained from a single population (Duncan *et al.* 1979; Nadeau *et al.* 1981). These observations suggest that many populations of house mice are sufficiently large for recombination to occur between closely linked loci and for recombinant chromosomes to have a reasonable chance of not being lost through genetic drift. Many genetic and ecological studies also suggest that mouse populations can be quite large (for a review, see Berry, 1981).

The apparent absence of disequilibrium between alleles of loci linked to the *t*-complex in wild mice is consistent with Rudolph & VandeBerg's study (1981) of *Ce-2* and *Pgk-2* polymorphisms in wild mice with a *t*-complex. Although disequilibrium between the t^{w5}-complex and *Pgk-2*^{c} was found in their study, the t^{w5}-complex was also associated with several combinations of *Ce-2* and *Pgk-2* alleles. Because *t*-complexes in other populations are associated with other alleles of *Pgk-2* (Table 1), the disequilibrium that they observed probably resulted from sampling related individuals rather than from natural selection favouring an association between *Pgk-2* and the *t*-complex. Furthermore, the *Pgk-2* data presented in Table 1 disprove the hypothesis (Rudolph & VandeBerg, 1981) that homozygosity for *Pgk-2*^{c} accounts for male sterility. For example, the t^{w2}- and t^{w8}-complexes both belong to the t^{w2} complementation group and produce similar patterns of sterility in homozygous males (Dunn & Suckling, 1956). Nevertheless, the t^{w2}-complex was associated with *Pgk-2*^{c} and the t^{w8}-complex with *Pgk-2*^{a}, indicating that homozygosity of the *Pgk-2*^{c} allele is not required for producing male sterility.

A number of hypotheses have been proposed to account for gametic disequilibrium between the *t*-complex the *H-2* complex and *Tcp-1*; these hypotheses can now be re-evaluated to take into consideration the apparent absence of disequilibrium between the *t*-complex and linked allozyme-encoding loci. The first hypothesis is that the *t*-complex originates from a species other than the house mouse. It has been hypothesized that in the species in which it originated, the *t*-complex contributes to normal embryonic development, but in the house mouse the *t*-complex results in lethality or, in certain cases, male sterility (Silver, 1982). This hypothesis is based in part on the observation that alleles of a number of loci including *Tcp-1* are found only in mice with a *t*-complex and not in other mice (Silver *et al.* 1980; L. M. Silver, personal communication). Also supporting this hypothesis is the observation that recombination is not suppressed in mice heterozygous for complementing *t*-complexes, but is suppressed in mice heterozygous for *t*-bearing and wild-type chromosomes (Silver & Artzt, 1981). In the present survey, alleles of allozyme-encoding loci unique to *t*-bearing chromosomes were not found. Thus these data do not support Silver's hypothesis, although they do not disprove it. Furthermore, if Silver's hypothesis is correct, the chromosome segment involved probably does not include *C-3*, *Ce-2* and *Pgk-2*, since none of these loci shows disequilibrium with the *t*-complex (Table 1) and recombination is

not suppressed between each of these loci and the *t*-complex (J. H. Nadeau, in preparation).

Another hypothesis is that gametic disequilibrium is maintained by natural selection favouring certain combinations of alleles of loci linked to the *t*-complex (cf. Hammerberg & Klein, 1975*a*). The results of the present survey suggest that, if this hypothesis is correct, selection responsible for maintaining disequilibrium acts specifically on the *t*- and *H-2* complexes (or on very closely linked loci), but not on the linked allozyme-encoding loci. It has also been hypothesized that one facet of the interaction between the *t* and *H-2* complexes is that the *t*-complex enhances heterozygosity of the *H-2* complex (Snell, 1968). This hypothesis can be rejected because *H-2* heterozygosity approaches 100% in mice without a *t*-complex (Duncan *et al.* 1979; Nadeau *et al.* 1981). In fact, because of disequilibrium between the *t* and *H-2* complexes, *H-2* heterozygosity is decreased in populations in which a *t*-complex is present.

The final hypothesis to account for disequilibrium between the *t*-complex, the *H-2* complex and *Tcp-1*, but not between the *t*-complex and linked allozyme-encoding loci, involves recombination suppression (Hammerberg & Klein, 1975*a*, *b*). An example of the influence of the *t*-complex on recombination is that the recombination frequency between *T* and the *H-2* complex is about 0·5% when a *t*-bearing chromosome is present, whereas the frequency is 11% in wild-type chromosomes (Hammerberg & Klein, 1975*b*). It is well established that the rate of decay of disequilibrium depends very closely on recombination frequency (Weinberg, 1909; Jennings, 1917; Robbins, 1918; Geiringer, 1944). For example, for loci such as *C-3*, *Ce-2*, *Glo-1* and *Pgk-2*, where the recombination frequency between a given locus and the *t*-complex is 5% or more (J. H. Nadeau, in preparation), less than 10% of the original disequilibrium is expected to remain after 50 generations. It was therefore not surprising that disequilibrium was not observed between these loci and *t*-complexes maintained in laboratory colonies for many years. By contrast, disequilibrium involving *Tcp-1* is expected given its very low recombination frequency with the *t*-complex (Silver *et al.* 1980). Disequilibrium involving *H-2* is more difficult to explain, however. The recombination frequency between the *t* and *H-2* complexes varies between 0 and 1·3%, depending on the cross and the *t*-complex involved (Hammerberg & Klein, 1975*b*). If a frequency of 0·5% is assumed, it can be shown that less than 10% of the original disequilibrium is expected to remain after 500 generations. Although recombination suppression slows the rate of decay of disequilibrium, these calculations suggest that some other factor such as natural selection is involved in maintaining disequilibrium.

In addition to providing information about the mechanisms maintaining gametic disequilibrium between the *t*-complex, the *H-2* complex and *Tcp-1*, the polymorphisms of these allozyme-encoding loci can be used in genetic studies for determining order of loci linked to the *t*-complex and for studying the influence of the *t*-complex on recombination between linked loci. Although the order of *T*, *tf* and *H-2* in wild-type chromosomes is as given in Fig. 1, Artzt, Shin & Bennett (1982) have presented evidence suggesting that the *H-2* complex is located centromeric to *tf* in many chromosomes bearing a *t*-complex. This result suggests that one or more chromosome rearrangements are associated with the *t*-complex.

The polymorphisms of loci linked to the *t*-complex can be used for determining whether other loci are located in anomalous locations in *t*-bearing chromosomes and for characterizing the number, kind and size of chromosomal rearrangements associated with the *t*-complex. Moreover, although recombination is suppressed between the *t* and *H-2* complexes, but not between the *t*-complex and thin fur which is located telomeric to *C-3* in wild-type chromosomes (Hammerberg & Klein,

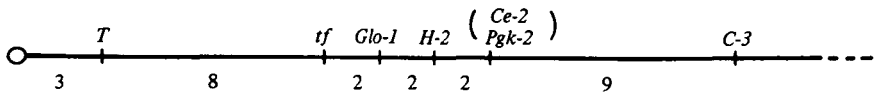

Fig. 1. Linkage map of markers on a wild-type Chromosome 17 of the house mouse. The markers included are brachyury (*T*), which is allelic to the *t*-complex, tufted (*tf*), glyoxalase-1 (*Glo-1*), histocompatibility complex-2 (*H-2*), kidney catalase (*Ce-2*), phosphoglycerate kinase-2 (*Pgk-2*) and complement component-3 (*C-3*). The *t*-complex is located in the interval marked by *T* and *tf*. *Tcp-1* is located within the *t*-complex. The centromere is located at the left end of the chromosome as diagrammed. Parentheses around *Ce-2* and *Pgk-2* indicate that the order of these markers is not certain. Distances are given in centiMorgans.

1975*b*), it is not known whether recombination suppression includes other loci located between the *H-2* complex and thin fur. The polymorphisms of allozyme-encoding loci linked to the *t*-complex can be used for determining whether recombination between these loci and the *t*-complex is suppressed (J. H. Nadeau, in preparation).

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