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T(16: 17)43H translocation as a tool in analysis of the proximal part of chromosome 17 (including *T-t* gene complex) of the mouse*

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SUMMARY

Linkage relationships of three gene markers of chromosome 17, namely *Brachyury* (*T*), *tufted* (*tf*), and *Histocompatibility-2* (*H-2*), to the breakpoint of *T(16;17)43H* male sterile translocation were established. The following order was found: *T–tf–T43H–H-2*. In all cases the translocation break was found in cis to $H\text{-}2^k$, haplotype, no recombinant being found among 218 backcross individuals examined. More than 60 viable and fertile animals trisomic for the proximal part of chromosome 17 (including *T-t* genetic complex) have been recovered among progeny of *T43H*/+ female translocation heterozygotes as a result of adjacent –2 disjunction at first meiotic division. Mutation *tf* has been assigned to band 17B in chromosome 17 by comparing the location of *T190Ca* and *T43H* genetic and cytological breakpoints. Recombination between centromere 17 and *T43H* break was reduced almost to zero in the presence of *Rb(16.17)7Bnr* translocation. The unexpected restoration of male fertility was observed in *T43H/Rb7Bnr* hybrids (*T43H*/+ males being completely sterile) which made it possible to prepare the first homozygotes for *T43H* male-sterile translocation. Direct estimation of chiasma frequencies in centromere 17–*T43H* region indicated an 11 cM distance between the centromere 17 and the proximal end of t^{12} haplotype. The significance of centromere –*t* (or *H-2*) distance on the predictable restrictions of the possible haploid manifestation of *T-t* or *H-2* gene products on sperm membrane is discussed.

1. INTRODUCTION

The proximal part of chromosome 17 of the mouse, *Mus musculus* L., carries two of the most complex and polymorphic genetic systems hitherto known in mammals: the *T-t* system involved in the embryonic development and spermatogenic differentiation, and the major histocompatibility system, *H-2* (for review see Bennet, 1975; Klein & Hammerberg, 1977; Klein, 1975; Snell, Daussett & Nathenson, 1976). Recently a reciprocal translocation *T(16; 17)43H*, marking

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this part of chromosome 17, has been recovered by Searle, Beechey & Evans (1978). One breakpoint of the *T43H* male-sterile translocation disrupts the centromeric heterochromatin of chromosome 16 while the other break is located in the middle part of the chromosome 17 (Searle, Beechey & Evans, 1978).

In this communication a complete genetic linkage between *T43H* breakpoint and *H-2* complex is described together with linkage relationship of some other gene markers of the chromosome 17. An attempt to determine genetically the proximal (centromeric) end of the *T-t* complex on chromosome 17 and the recovery of viable and fertile animals displaying three doses of genes of the *T-t* complex are presented as the first results of applying the *T43H* translocation to the study of organization and functions of the murine chromosome 17.

2. MATERIALS AND METHODS

(i) *Mice*

Breeding nuclei of mice heterozygous for *T(16;17)43H* translocation and homozygous for Robertsonian translocation *Rb(16.17)7Bnr* were obtained through the courtesy of Dr A. G. Searle, MRC Radiobiology Unit, Harwell, England, and Dr J. Klein, The University of Michigan School of Medicine, Ann Arbor, Michigan, respectively. For the origin of these translocations see Searle *et al.* (1978) and Klein (1971). The inbred and congenic resistant strains C57BL/10ScSnPh (B10), B10.D2, B10-T and non-inbred *T tf/+tf* and *T tf/t*^{12}+ stocks are maintained in this Institute.

(ii) *Cytogenetic methods*

Mice which could be sacrificed were tested for the presence of translocation in chromosome preparations of bone marrow. Mice intended for further breeding were treated with 0·1 ml of complete Freund's adjuvant (Difco) i.p. and 6 days later they were splenectomized under Nembutal (Abbott) anaesthesia. In all cases the presence of translocation was determined by examination of mitotic preparations stained for C-binding as described previously (Forejt, 1973*a*). The same staining technique was applied to air-dried preparations of meiotic chromosomes (Evans, Breckon & Ford, 1964).

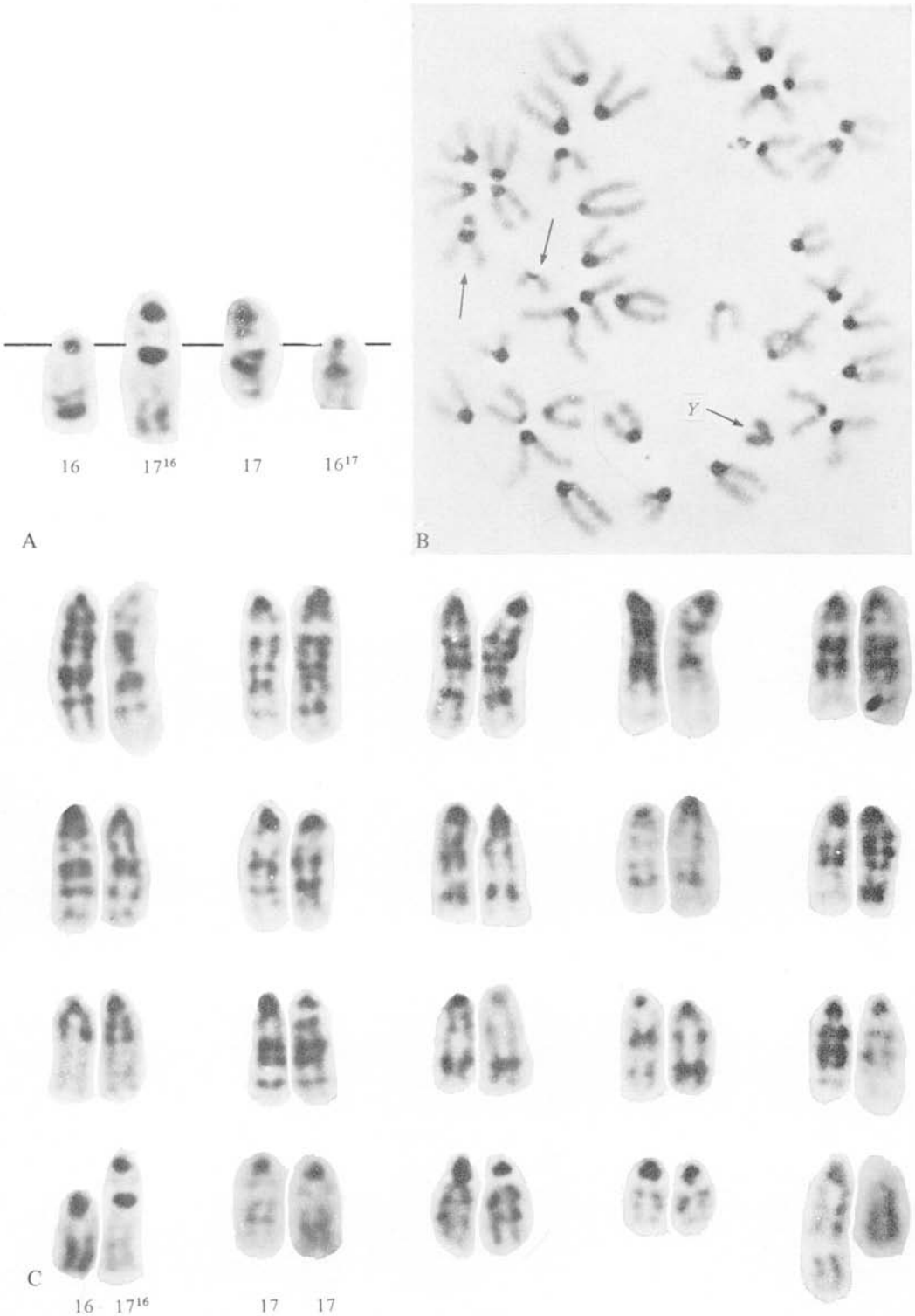
(iii) *Serotyping of* H-2 *antigens*

The H-2 antigens were determined by PVP haemagglutination technique (Stimpfling, 1961) and by microcytotoxicity test (Micková & Iványi, 1976).

3. RESULTS

(i) *Cytological identification of* T43H *translocation in mitosis and meiosis*

Both products of reciprocal translocation between chromosomes 16 and 17 can be easily identified in mitosis after C- or G-banding (Plate 1). Chromosome 17^{16} (possessing centromere 17) is characterized by the presence of an interstitial C-band derived from the distal part of centromeric heterochromatin of chromo-



Mitotic chromosomes of mice of the genotypes *T43H*/+ and *Ts(17A1-17B)43H*. (A) G-banded chromosomes involved in *T43H* translocation. (B) C-banded mitosis of *T43H*/+ male. Translocated chromosomes are shown by arrows. (C) G-banded karotype of *Ts43H* male.

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some 16, while the second product of the translocation, the chromosome 16^{17}, is distinguished as the smallest chromosome of the complement differing from the *Y* chromosome by a tiny C-band. G-band analysis of mitotic chromosome, confirmed the location of breakpoints to bands 17B and 16A1 (Evans, Searle & Beechey, 1977) (Plate 1). In meiosis the translocation configuration can be precisely identified by using C-band staining. Moreover, the frequency of chiasma formation between centromere 17 and *T43H* breakpoint can be determined directly by scoring cells with ChIV and II + II configurations (see below).

(ii) *Genetic distances between* T43H *translocation breakpoint and* T, tf *and* H-2 *gene loci*

The linkage relationship between *T43H* break and the gene loci of the chromosome 17 was studied in 5 different test-crosses: 3 two-point test-crosses (that is, *T–T43H*, *tf-T43H*, *T43H-H-2*) and 2 three-point test crosses (that is, *T-tf-T43H* and *T-T43H-H-2*) as shown in Tables 1–5. Mapping of the *H-2* complex with respect to *T43H* (Table 4 and 5) was performed by analysing the progeny of the first three backcross generations aimed at transferring the *T43H* translocation

Table 1. *Recombination between* T *and* T43H *breakpoint*

	Offspring				
Cross	*+T43H*	*T+*	*T T43H*	*++*	Total
+T43H/T+ × *++/++*	18	37	8	9	72
T T43H/++ × *++/++*	0	3	3	5	11
Total					83

Recombination: (% ± S.E.) 24·1 ± 4·7.

Table 2. *Recombination between* tf *and* T43H *breakpoint*

	Offspring				
Cross	*+T43H*	*tf+*	*tf T43H*	*++*	Total
+T43H/tf+ × *tf+/tf+*	42	28	1	1	72

Recombination: (% ± S.E.) 2·8 ± 1·9.

on the C57BL/10 strain genetic background. The parent carrying the translocation was always female in the experiments described here because of the sterility of the *T43H/+* males. The transmission of *T43H* to progeny varied in different crosses, the statistically significant excess of *T43H/+* heterozygotes being found in three-point test-cross *T–T43H–H-2* (Table 5). The biological significance of the abnormal segregation is unclear.

The *H-2* haplotype associated in cis position to the *T43H* breakpoint has been analysed in *T43H*(*H-2*?) × B10.D2(*H-2*^{d}) hybrids using a panel of defined anti *H-2* sera in microcytotoxicity tests on peripheral (lymph node) lymphocytes. It was found that the haplotype in question is indistinguishable from the *H-2*^{k}. The full description of the *H-2* haplotype analysis together with discovering a new

Table 3. *Progeny of three-point test cross of the type* T + T43H/+ tf +

T+	*T43H*	+*tf*	+ +	*T43H*	*T tf*	+	*T* + +	+ *tf T43H*	*T tf T43H*	+ + +	Total
21		21	2		6	0	1	0	0		51

Recombinations	% ± S.E.
T-T43H	17·6 ± 5·3
tf-T43H	2·0 ± 1·9
T-tf	15·7 ± 5·1

Table 4. *Recombination between* T43H *and* H-2^k

Cross	Offspring: *T43H H-2*^{k}	+ *H-2*^{b}	+ *H-2*^{d}	*T43H H-2*^{b}	*T43H H-2*^{d}	+ *H-2*^{k}	Total
T43H H-2^k/+ *H-2*^{b} × + *H-2*^{d}/+ *H-2*^{d}	53	64		0	0	0	117
T43H H-2^k/+ *H-2*^{d} × + *H-2*^{t}/+ *H-2*^{b}	18		16	0	0	0	34
Total	71	80		0	0		151

Recombination: 0%.

Table 5. *Progeny of three-point test cross of the type* +T43H H-2^k/T+H-2^b

+*T43H H-2*^{k}	*T*+*H-2*^{b}	*T T43H H-2*^{k}	+ + *H-2*^{b}	+*T43H H-2*^{b}	*T-H-2*^{k}	Total
34	16	8	9	0	0	67

Recombinations	% ± S.E.
T-T43H	25·4 ± 5·3
T43H-H-2	0·0
T-H-2	25·4 ± 5·3

intra *H-2* recombinant will be treated in a separate paper (Čapková & Forejt, in preparation).

The *H-2*^{k} haplotype is very closely linked with *T43H* break since no recombinant between these two chromosome points has been observed among 218 backcross animals examined (see Table 6 for summary of linkage data). The observation might indicate either a close physical association of the translocation break with *H-2* gene loci or the complete suppression of recombination between both markers.

(iii) *Production of partial trisomy 17 including the* T-t *chromosome region*

Viable partial trisomics carrying three doses of genes of the chromosome region between centromere 17 and *T43H* break were identified among the backcross individuals in the course of the genetic localization of the *T43H* breakpoint on the chromosome 17. The unbalanced genotype arose as a consequence of adjacent –2 disjunction at meiosis of females heterozygous for the *T43H* translocation. Plate 1 and Text-fig. 1 show that the trisomics lost the small translocation product, chromosome 16^{17}, but gained another chromosome 17 instead. The resulting

partial trisomy 17 cytologically confined to bands 17A1–17B is associated with monosomy for the proximal part of centromeric heterochromatin of chromosome 16. The partial monosomy can be expected to be phenotypically silent, since it involves satellite DNA, which is not transcribed *in vivo*.

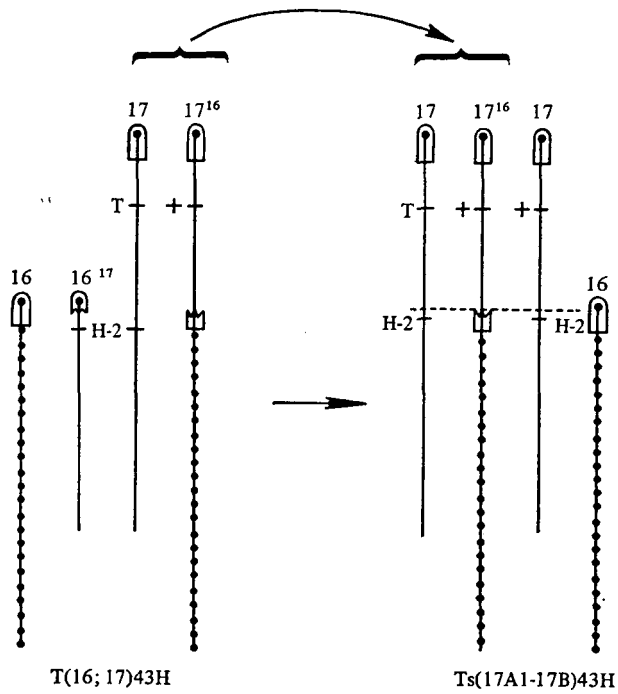

Fig. 1. Schematic representation of chromosomes involved in balanced *T43H* translocation and in partial trisomy *Ts(17A1-17B)43H*. The *H-2* haplotype is translocated to the close vicinity of broken centromeric heterochromatin (C-band) of chromosome 16^{17} in *T43H*/+ heterozygotes. In *Ts43H* the *H-2*^{k} is lost together with chromosome 16^{17} and three doses of *T-t* region are present. Partial trisomy is accompanied by monosomy for the proximal part of centromeric heterochromatin of chromosome 16. Drawing not to scale.

Table 6. *Map distances in* T–T43H *breakpoint region of chromosome 17 (Summary of data from Tables 1–5)*

	T	*tf*	*T43H*
H-2	25·4 ± 5·3	N.D.	0·0
T43H	22·9 ± 3·0	2·4 ± 1·4	
tf	15·7 ± 5·1		

Provided that the *H-2*^{k} were located proximally to *T43H* break – that is, between centromere 17 and *T43H* – then the trisomics would display three doses of *H-2* complex genes. On the contrary, if the *H-2*^{k} were located distally to *T43H*, then it would be lost in trisomics and only two doses of H-2 genes would be found. Serotyping specificities of 7 suitable trisomics pointed to the latter alternative; in crosses of the type *T43H H-2*^{k}/+ *H-2*$^b \times$ *H-2*^{d}/*H-2*^{d} each trisomic

was found to carry only two *H-2* haplotypes (*H-2*^{b} and *H-2*^{d}). The *H-2*^{k} was always lost together with the small translocation product, the chromosome 16^{17} (Text-fig. 1). Thus, the order of markers on chromosome 17 can be summarized as follows: centromere 17–*T*–*tf*–*T43H*–*H-2*, the whole *H-2*^{k} haplotype being locked on the 16^{17} marker chromosome.

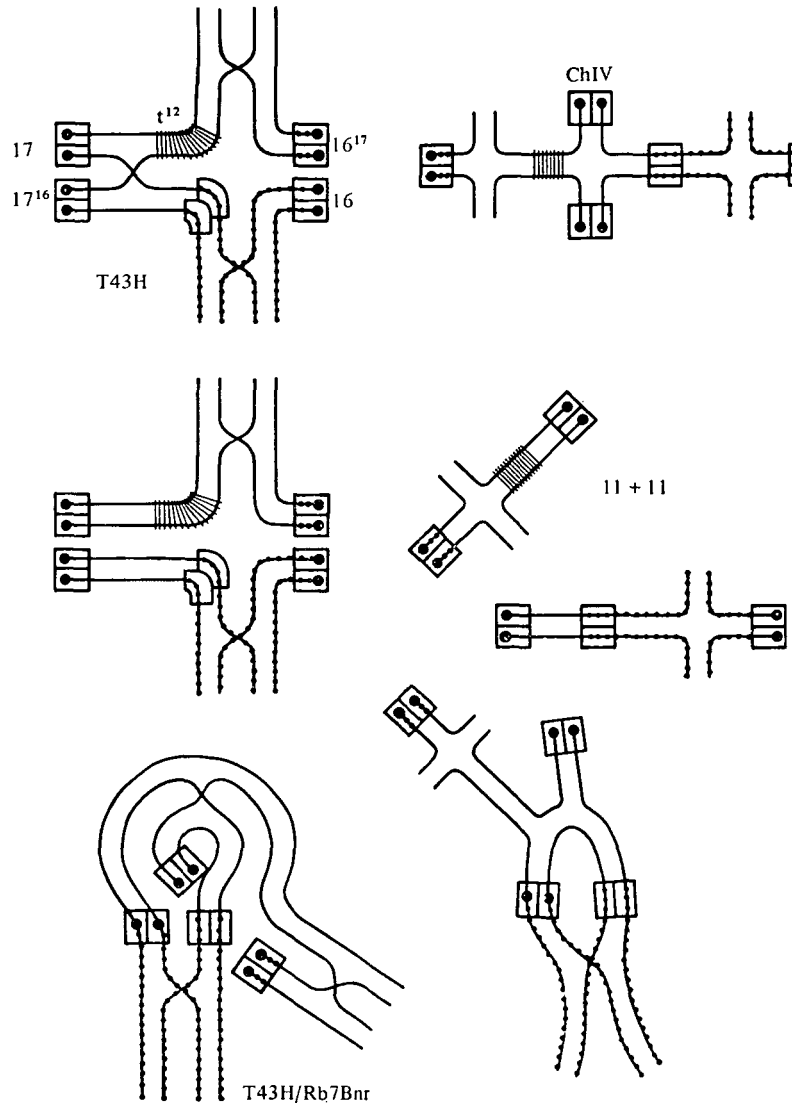

Fig. 2. Principle of meiotic analysis of recombination frequency between centromere 17 and *T43H* breakpoint in the presence of t^{12} haplotype or *Rb7Bnr* translocation. The schemes of pachytene pairing of translocated chromosomes are at the left, while the right part of the figure shows the schemes of resulting diakinesis-MI configurations, the frequency of which can be scored under the microscope. If the t^{12} reached the centromere 17 proximally, the ChIV configurations could not be expected to occur with $+T3H/t^{12}+$ genotype (cf. Table 7). Drawing not to scale.

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Up to the time of writing this manuscript more than 60 viable trisomics have been recovered among progeny of *T43H*/+ females with frequencies ranging from 0·0–0·15 in various crosses. At birth and during the first 2 weeks of postnatal life most of these trisomics were smaller than their normal sibs and an unidentified part of them died before weaning. Later, however, the difference disappeared and the trisomics were phenotypically indistinguishable from their normal sibs.

(iv) *The* t^{12} *haplotype and* Rb7Bnr *translocation influence chiasma formation in chromosome 17*

The C-band stained meiotic configurations of *T43H* translocation can be readily distinguished in diakinesis – MI plates. Text-fig 2. shows the scheme of pachytene pairing of chromosomes involved in the translocation cross and the effect of genetic recombination in the arms of the pachytene cross on chiasma formation at diakinesis. Thus, the recombination in centromere 17 – *T43H* break region results in the formation of 'Chain-of-four' (ChIV) translocation quadrivalent, while the absence of crossing-over in this region is signalled by the formation of a II + II configuration.

Table 7. *Meiotic recombinations between centromere and* T43H *breakpoint on the chromosome 17*

Expt. *	Genotype †	Translocation configuration						Recombination (%) from centromere to *T43H* breakpoint
		Ring	Chain	II + II	Total	Ring %	Chain %	
1	+ *T43H*/*T*+	—	276	124	400	—	69·0	34·5
2	+ *T43H*/t^{12}	—	77	274	351	—	21·9	11·0
3	+ *T43H*/*Rb7*	14	356	—	370	3·8		1·9

* Data from Expts 1 and 2 recalculated from Forejt & Gregorová (1977).

† Expt. 1 includes also + *T43H*/t^{121} males. t^{121} haplotype is a viable recombinant haplotype (from parental t^{12}) not suppressing recombination.

As shown in section (ii), the *T43H* breakpoint lies near the proximal end (*K*-end) of the *H-2* complex, being located inside the region of the crossover suppressive effect exerted by recessive lethal *t* haplotypes (t^1) (Hammerberg & Klein, 1975*a*, *b*). Therefore, by estimating the chiasma frequency between centromere 17 and *T43H* breakpoint in + *T43H*/t^1+ hybrids, information could be obtained on the genetic distance between the centromere and the proximal end of t^1 haplotype. In this way the proximal border of the *T-t* genetic complex could be determined. Table 7 shows the results of the meiotic analysis of + *T43H*/t^{12}+ and + *T43H*/+ + males. The frequency of chiasma formation in the centromere 17–*T43H* region of chromosome 17 was 0·69 in the absence of t^{12}, corresponding to a map distance of 34·5 cM. Introduction of t^{12} in trans to *T43H* break caused a significant reduction of this map distance but not its complete elimination which would be expected if the t^{12} suppressed recombination up to the centromere 17. It can be concluded that in *T43H*/t^{12}+ hybrids the crossover suppression effect

caused by the t^{12} haplotype does not reach proximally the centromere 17 but stops 11 map units before it.

While this conclusion is in good agreement with the previous indirect evidence based on total chiasma frequencies of translocation multivalents of heterozygotes for *T(1:17) 190Ca* and *(T9;17)138Ca* translocations (Forejt, 1972; Lyon *et al.* 1979), it differs from the data obtained in crosses where the *Rb(16.17)7Bnr* Robertsonian translocation was used as a centromere marker (Klein, 1971; Forejt, 1973*b*; Hammerberg & Klein, 1975*a*). Much lower values were obtained in the latter case (2-4 cM) and it has been tacitly assumed that recessive lethal *t* haplotypes occupy the whole proximal part of chromosome 17 starting from the centromere (Bennett, 1975; Klein & Hammerberg, 1977). A possible explanation of the difference between both estimates could consist in suppression of recombination caused by *Rb7Bnr* on the centromeric side of chromosome 17. Such a phenomenon has been demonstrated in some other Robertsonian translocations derived from the same source as *Rb7Bnr*, that is from Mus musculus poschiavinus (Cattanach, 1978). For this reason, $+T43H/Rb7Bnr+$ male hybrids were examined for chiasma frequencies in the centromere 17–*T43H* breakpoint region and almost complete suppression of recombination (2% instead of 35%, Table 7) has been found. It has to be admitted, however, that the interpretation of this observation is by no means unequivocal because at least part of the crossover suppression effect can be due to the possible pairing difficulties of translocated chromosomes at pachytene (Text-fig. 2). An unexpected by-product of this experiment has been the observation of restoration of male fertility in $+T43H/Rb7Bnr+$ hybrids which enabled us to prepare the first viable and fertile animals homozygous for the *T43H* male–sterile translocation (Forejt & Gregorová, unpublished).

4. DISCUSSION

(i) T43H *translocation in the study of organization and function of the chromosome 17*

The *T43H* translocation displays several unique properties which make it a powerful cytogenic tool for studying the organization and function of chromosome 17: (1) The *T43H* breakpoint separates physically both major genetic complexes, *T-t* and *H-2*, the position of the breakpoint being signalled by an interstitial C-band in the rearranged 17^{16} chromosome. (2) *T-t* and *H-2* complexes segregate independently in *T43H/T43H* homozygous animals, the *H-2* complex being located on the smallest chromosome pair of the complement. (3) Transfer of the *H-2* complex from the euchromatic part of the chromosome to the close vicinity of broken centromeric heterochromatin makes the *H-2* genes the potential candidates for testing the position effect variegation (Baker, 1968) in a mammalian chromosome. (4) Adjacent-2 disjunction in females heterozygous for *T43H* leads to the production of gamates giving rise to zygotes either trisomic or monosomic for the proximal part of chromosome 17.

The trisomy for the whole chromosome 17 causes the early death of embryos

between 8th and 10th day of prenatal development (Baranov & Dyban, 1972; Gropp, 1975; Dyban & Baranov, 1978). The recovery of viable and fertile animals trisomic for the proximal part of chromosome 17 demonstrates *per se* that the *T-t* 'developmental' gene complex is not itself responsible for embryonic lethality of trisomics carrying three doses of the whole chromosome 17. This conclusion is in good agreement with the previous finding by Lyon (1978) of viable tertial trisomy derived from the *T(9;17)190Ca* translocation and including the centromere 17–*tf* region. The study of interactions between various *t* haplotypes and alleles of the *Hst-1* gene (Forejt & Iványi, 1975) in trisomic condition is in progress.

(ii) *Regional assignments of* T-t *and* H-2 *gene complexes and* tf *mutation in the cytological map of chromosome 17*

Chromosome 17 stained by the G-banding technique displays 11 bands – 6 dark and 5 light. This cytological map can be related, more or less precisely, to the genetic map of the chromosome, by means of three reciprocal translocations

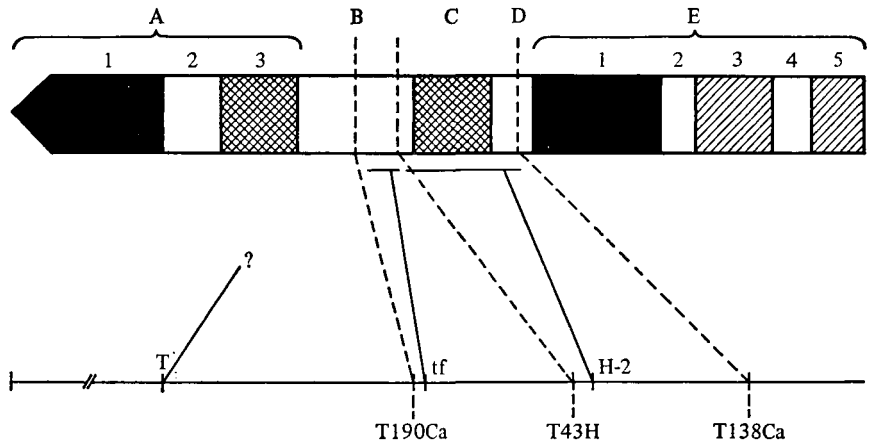

Fig. 3. Regional assignments of major gene markers to G-bands of chromosome 17 by means of *T190Ca*, *T43H*, and *T138Ca* translocations.

crosslinking both maps (Text-fig. 3). Breakpoints of the translocations *T190Ca* and *T43H* were both located to band 17B (Eicher & Washburn, 1977; Evans *et al.* 1977). The *tf* mutation maps distally to *T190Ca* (Lyon, 1978) but proximally to *T43H* (this paper), hence it has to be located between the *T190Ca* and *T43H* breakpoints in band 17B. Assignment of the *H-2* region is more complicated. Obviously, it could be located also in band 17B since no recombination has been observed between *T43H* and *H-2*. However, *H-2* could be assigned as well two bands distally, to band 17D near the *T138Ca* translocation breakpoint since only 3% of recombination has been found between *H-2* and *T138Ca* by Klein & Klein (1972).

Location of the *T43H* breakpoint in respect of *T* and *tf* genes has been recently achieved by Beechey & Searle (1978). The authors found the same order of markers

as presented in this paper, but they observed a considerably higher frequency of recombination in the *tf–T43H* region. The reason for the difference is unclear.

The available data do not permit unequivocal assignment of the whole *T-t* complex to the cytological map of chromosome 17. Nevertheless, at least the lethality factor of t^6 haplotype can be assigned to band 17B due to its close genetic linkage with the *tf* gene locus (Lyon & Meredith, 1964; Lyon & Mason, 1977) which has been proved to lie in 17B (cf. above).

(iii) *Recessive lethal* t *haplotypes do not begin from the centromere of chromosome 17*

Most of the recessive lethal *t* haplotypes suppress recombination between the *T* and *H-2* loci (Hammerberg & Klein, 1975*a*, *b*). In principle, the suppression of recombination may be due to failure of crossing-over formation or to the elimination of crossovers when normal crossing over occurred. The former alternative has been experimentally supported by demonstrating that various lethal *t* haplotypes reduced formation of chiasmata in the proximal part of chromosome 17 (Forejt, 1972; Forejt & Gregorová, 1977; Lyon *et al.* 1979). Furthermore, genetic evidence has been provided, indicating the coincidence between the *t* chromatin

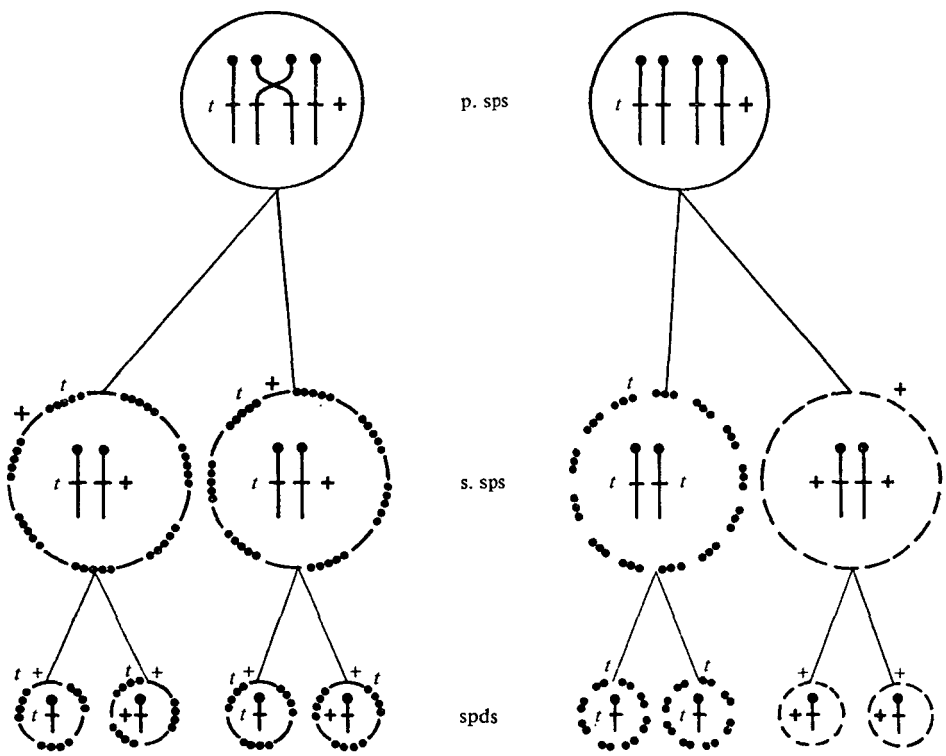

Fig. 4. The expected effect of recombination between centromere 17 and *a t* gene (or genes) coding for the presumed cell surface antigen (s) on the detection of haploid expression of this gene in secondary spermatocytes (s.sps), spermatids (spds) or sperm. For the sake of simplicity, the gene is considered to be expressed only in secondary spermatocytes. p.sps – pachytene spermatocytes.

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and the location of recombination suppression in such a way that the extent of recombination suppression might reflect the length of the chromosome segment occupied by the *t*-chromatin (Lyon *et al.* 1979).

These data together with recently obtained direct proof of partial chiasmatype theory (namely, visualization of homologous chromatid exchanges in the chiasmata – Tease, 1978; Polani *et al.* 1979) enabled us to infer the location of the centromeric end of t^{12} haplotype from chiasma frequency analysis. The calculated distance between centromere and t^{12} haplotype, 11 cM is in good agreement with the previous finding of 13 cM distance between the same two points performed by means of the *T(9;17)190Ca* translocation (Forejt, 1972). It has to be admitted that the frequency of recombination between centromere and t^{12} haplotype could be enhanced in comparison with recombination in the same area of an intact chromosome 17 for the following reasons: (i) translocations of chromosome 17 enhance recombination in the interstitial segment (Lyon & Phillips, 1959; Klein & Klein, 1972), and (ii) Bennet *et al* (1979) have recently shown that recombination is enhanced in a region immediately distal to the t^{38}, haplotype.

The location of the *T-t* haplotype with respect to centromere 17 has an important bearing on predictable restrictions concerning the possible haploid *t* (and *H-2*) gene product expression on sperm cell membrane. As shown in Text-fig. 4, the haploid expression of the t^{12} can be expected if the relevant gene is transcribed in the course of spermatogenic differentiation not earlier than at spermatid stage. An earlier transcription in the secondary spermatocytes would result in expression of both allelic forms in those sperm cells that are derived from primary spermatocytes where recombination occurred between centromere 17 and the t^{12} haplotype. Similarly, when considering, for example, 30 % of recombination between centromere 17 and *H-2* (in the absence of a *t* haplotype), then only 20 % of sperm cells would display the haploid expression of one *H-2* haplotype, while 60 % of spermatozoa would display H-*2* antigens of both haplotypes present in diploid precursor. It may be worthwhile mentioning at this place that several authors obtained a strong indication of *H-2* expression as early as in primary spermatocytes (Vojtíšková & Pokorná, 1972; Vojtíšková *et al.* 1974; Fellous *et al.* 1976; Erickson, 1977). Moreover, the presence of F9 antigen – presumably a product of + t^{12} haplotype – has been observed in all forms of male germ cells (Gachelin *et al.* 1976). Thus, in order to maintain the concept of *T-t* and *H-2* haploid expression, a fast turnover of the cell surface determinants on the differentiating cells should be envisaged and the premise of *T-t* and H-*2* gene transcription at spermatid stage should be postulated. Then, irrespective of the position of their loci on the chromosome, the haploid *T-t* and *H-2* gene products might be present on the membrane of sperm cells.

REFERENCES

Baker, W. K. (1968). Position-effect variegation. *Advances in Genetics*. **14**, 133–169.

Baranov, V. S. & Dyban, A. P. (1972). Embryonic damage of trisomic offsprings of mice with Robertsonian translocation (centric fusion T1 Iem. *Archiv Anatomii Histologii i Embryologii* **63**, 67–77 (in Russian).

BEECHEY, C. V. & SEARLE, A. G. (1979). Private communication. *Mouse News Letter*, p. 59.
BENNETT, D. (1975). The *t*-locus of the mouse. *Cell* **6**, 441–454.
BENNETT, D., ARTZT, K., COOKINGHAM, J. & CALO, C. (1979). Recombinational analysis of the viable t-haplotype t^{38}. *Genetical Research* **33**, 269–277.
CATTANACH, B. M. (1978). Crossover suppression in mice heterozygous for tobacco mouse metacentrics. *Cytogenetics and Cell Genetics* **20**, 264–279.
DYBAN, A. P. & BARANOV, V. S. (1978). *Cytogenetics of Development in Mammals*. Nauka, Moscow (in Russian).
EICHER, E. M. & WASHBURN, L. (1977). Private communication. *Mouse News Letter* **56**, 43.
ERICKSON, R. P. (1977). Gene expression of a region of chromosome 17 during murine spermatogenesis. *Journal of Immunogenetics* **4**, 353–362.
EVANS, E. P., BRECKON, G. & FORD, C. E. (1964). An air-drying method for meiotic preparations from mammalian testes. *Cytogenetics* **3**, 289–294.
EVANS, E. P., BEECHEY, C. V. & SEARLE, A. G. (1977). Private communication. *Mouse News Letter* **57**, 17.
FELLOUS, M., ERICKSON, R. P., GACHELIN, G. & JACOB, F. (1976). The time of appearance of Ia antigens during spermatogenesis in the mouse. *Transplantation* **22**, 440–444.
FOREJT, J. (1972). Chiasmata and crossing-over in the male mouse (*Mus musculus*). Suppression of recombination and chiasma frequencies in the ninth linkage group. *Folia Biologica* (*Praha*) **18**, 161–170.
FOREJT, J. (1973*a*). Centromeric heterochromatin polymorphism in the house mouse. Evidence from inbred strains and natural populations. *Chromosoma* **43**, 187–201.
FOREJT, J. (1973*b*). Private communication. *Mouse News Letter* **49**, 45.
FOREJT, J. & GREGOROVÁ, S. (1977). Meiotic studies of translocations causing male sterility in the mouse. I. Autosomal reciprocal translocations. *Cytogenetics and Cell Genetics* **19**, 159–179.
FOREJT, J. & IVÁNYI, P. (1975). Genetic studies of male sterility of hybrids between laboratory and wild mice. (*Mus musculus* L.). *Genetical Research* **24**, 189–206.
GACHELIN, G., FELLOUS, M., GUENET, J. L. & JACOB, F. (1976). Developmental expression of an early embryonic antigen common to mouse spermatozoa and cleavage embryos, and to human spermatozoa: its expression during spermatogenesis. *Developmental Biology* **50**, 310–320.
GROPP, A. (1975). Chromosomal animal model of human disease. Fetal trisomy and developmental failure. *Teratology*, pp. 17–31. Berlin: Springer-Verlag.
HAMMERBERG, C. & KLEIN, J. (1975*a*). Linkage disequilibrium between H-2 and t complexes in chromosome 17 of the mouse. *Nature* **258**, 296–299.
HAMMERBERG, C. & KLEIN, J. (1975*b*). Linkage relationships of markers on chromosome 17 of the house mouse. *Genetical Research* **19**, 203–211.
KLEIN, J. (1971). Cytological identification of the chromosome carrying the IXth linkage group (including H-2) in the house mouse. *Proceedings of the National Academy of Sciences, U.S.A.* **68**, 1594–1597.
KLEIN, J. (1975). *Biology of the Mouse Histocompatibility-2 Complex*. New York: Springer-Verlag.
KLEIN, J. & HAMMERBERG, C. (1977). The control of differentiation by the T complex. *Immunological Reviews* **33**, 70–104.
KLEIN, J. & KLEIN, D. (1972). Position of the translocation break T(2:9)138Ca in linkage group IX of the mouse. *Genetical Research* **19**, 177–179.
LYON, M. F., EVANS, E. P., JARVIS, S. E. & SAYERS, I. (1979). t-haplotypes of the mouse may involve a change in intercalary DNA. *Nature* **279**, 38–42.
LYON, M. F. (1978). Private communication. *Mouse News Letter* **58**, 44.
LYON, M. F. & PHILIPS, R. J. S. (1959). Crossing-over in mice heterozygous for t-alleles. *Heredity* **13**, 23–32.
LYON, M. F. & MASON, I. (1977). Information on the nature of t haplotypes from the interaction of mutant haplotypes in male fertility and segregation ratio. *Genetical Research* **29**, 255–266.
LYON, M. F. & MEREDITH, R. (1964). Investigation of the nature of t-alleles in the mouse. I. Genetic analysis of a series of mutants derived from a lethal allele. *Heredity* **19**, 301–312.

Micková, M. & Iványi, P. (1976). Study of H-2 antigens of wild mice (*Mus musculus* L.). *Folia Biologica* (*Praha*) **22**, 169–189.

Polani, P. E., Crolla, D. A., Seller, M. J. & Moir, F. (1979). Meiotic crossing-over exchange in the female mouse visualized by BUdR substitution. *Nature* **278**, 348–349.

Searle, A. G., Beechy, C. V. & Evans, E. P. (1978). Meiotic effects in chromosomally derived sterility of mice. *Annales de Biologie animale Biochemie et Biophysique* **18** (2B), 391–398.

Snell, G. D., Daussett, J. & Nathenson, S. G. (1976). *Histocompatibility*. New York: Academic Press.

Stimpfling, J. H. (1961). The use of PVP as a developing agent in mouse hemagglutination test. *Transplantation Bulletin* **27**, 109–111.

Tease, C. (1978). Cytological detection of crossing-over in BUdR substituted meiotic chromosomes using the fluorescent plus Giemsa technique. *Nature* **272**, 823–824.

Vojtíšková, M., Pokorná, Z., Viklický, V. boubelík, M. & Hattikudur, N. S. (1974). The expression of H-2 and differentiation antigens on mouse spermatozoa. *Folia Biologica* (*Praha*) **20**, 321-324.

Vojtíšková, M. & Pokorná, Z. (1972). Developmental expression of H-2 antigens in the spermatogenic cell series: possible bearing on haploid gene action. *Folia Biologica* (*Praha*) **18**, 1–9.