INVESTIGATIONS OF THE NATURE OF t -ALLELES IN THE MOUSE

II. GENETIC ANALYSIS OF AN UNUSUAL MUTANT ALLELE AND ITS DERIVATIVES

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THE previous paper in this series described the genetic analysis of a group of mutant t -alleles, derived from the allele t^6 . Of the 11 mutants available for study, 10 had obviously arisen through crossing-over in the abnormal chromosome region present in t^6 , and these were all described. The remaining one, t^{h7} , had not obviously arisen through crossing-over, and showed a different T -modifying effect from t^6 . The genetic analysis of this mutant, and of a group of alleles derived from it, are described in the present paper.

1. ORIGIN AND PRELIMINARY TESTS OF THE MUTANT ALLELE t^{h7}

As mentioned in the earlier paper the original mutant animal carrying the allele t^{h7} was a non-tufted normal-tailed animal which arose in a tailless balanced lethal line, $Ttf/t^6+ \times Ttf/t^6+$, and which was shown to have the genotype $Ttf/t^{h7}+$. At first t^{h7} was thought to be a wildtype allele, *i.e.* one which gave a short-tailed phenotype when in combination with the gene T . The usual tests were started with it, and in particular, presumed Tt^{h7} animals were mated together, to test the viability of $t^{h7}t^{h7}$. These matings gave far fewer short-tailed and more normal-tailed young than expected (table 1), and moreover the normal-tailed offspring, at first taken to be of the genotype $t^{h7}t^{h7}$, all proved on genetical test to be carrying T . Five such animals were tested. These results showed that the action of T was being suppressed, either through some effect of the general genetic background, or by the new allele t^{h7} itself. If t^{h7} were responsible the suppressing effect should show linkage with tf . This was tested by crosses in which $+tf/t^{h7}+$ and $Ttf/t^{h7}+$ animals were mated to $Ttf/+tf$ (table 1). Among the progeny there was a shortage of the short-tailed non-tufted type, which would be expected to carry t^{h7} , and a compensating excess of normal-tailed non-tufted, whereas in the tufted class the expression of T was apparently normal. This was taken as indicating linkage of the suppressing effect with tf , and hence that the new allele was probably responsible. Thus t^{h7} differed from all previously known t -alleles in its T -modifying effect, in that it suppressed the action of T

TABLE 1
The breeding behaviour of t^{h7}

Cross	Offspring			
	Short-tailed		Normal-tailed	
	+	tf	+	tf
$Ttf/t^{h7} + \times Ttf/t^{h7} +$	173	...	350	...
$+tf/t^{h7} + \times Ttf/+tf$	5	26	31	26
$Ttf/t^{h7} + \times Ttf/+tf$	9	29	42	...

rather than enhancing it. The other properties of this unusual allele were then studied.

2. PROPERTIES OF t^{h7}

(i) Viability of $t^{h7}t^{h7}$ and t^6t^{h7}

Tests of the viability of $t^{h7}t^{h7}$ have already been mentioned. No $t^{h7}t^{h7}$ animals were found among five normal-tailed young from these crosses which were genetically tested. Similarly, among the progeny

TABLE 2
Results of dissections of pregnant females carrying t^6 or t^{h7}

Lethal type expected	Genotype of parents		No. of ♀♀	Corpora lutea	Total implants	Normal implants	Small moles	Other	Per cent. moles
	♀	♂							
t^6t^6	Tt^6	Tt^6	9	81	60	26	28	6	46.7
t^6t^{h7}	Tt^6 $t^{h7}t^{h3}$	$t^{h7}t^{h3}$ Tt^6	7 7	64 56	43 49	23 23	18 24	2 2	45.7
$t^{h7}t^{h7}$	$t^{h7}t^{h3}$ or $+t^{h7}$	$t^{h7}t^{h3}$	13	109	95	57	34	4	35.8
None	$t^{h7}t^{h3}$ or $+t^{h7}$	$t^{h3}t^{h3}$	9	86	80	75	1	4	1.3

of crosses of $Tt^6 \times Tt^{h7}$, made to test the viability of t^6t^{h7} , the low proportion of normal-tailed relative to tailless young suggested that t^6t^{h7} also was lethal. This made it seem likely that t^{h7} carried the t^6 -lethal factor, and hence that $t^{h7}t^{h7}$, t^6t^{h7} and t^6t^6 embryos died from the same cause. To test this hypothesis female mice of suitable genotype, pregnant by suitable males, were dissected and their embryos were studied (table 2). The two points investigated were, firstly,

whether the number of dead embryos was consistent with death of the $t^{h7}t^{h7}$ and t^6t^{h7} types, and if so, secondly, whether the time of death of these types was the same as that of t^6t^6 . To prepare $t^{h7}t^{h7}$ embryos, females of type $t^{h7}t^{h3}$ or $+t^{h7}$ were mated to $t^{h7}t^{h3}$ males, and as a control similar females were mated to $t^{h3}t^{h3}$ males. (No lethal genotype was expected among the progeny of this latter cross, and hence it indicated the proportion of the embryonic death in the other crosses that could be ascribed to "spontaneous death".) To prepare t^6t^{h7} embryos, some crosses were made by mating similar females to Tt^6 males, and in others Tt^6 females were mated to $t^{h7}t^{h3}$ males, so that the females were of the same genotype as those in the crosses made to prepare t^6t^6 . The embryos were examined when 9-12 days old. The numbers of dead embryos were in accord with death of $t^{h7}t^{h7}$ and t^6t^{h7} , and also indicated that both these types were dying at the stage known as the "small mole". Embryos of type t^6t^6 also die at the "small mole" stage, and thus at first sight these data might seem to show that $t^{h7}t^{h7}$, t^6t^{h7} and t^6t^6 embryos had the same cause of death. However, since "small moles" are left by embryos dying at any stage from implantation to about 8 days' gestation it is possible that the three genotypes may have died at different times during this period. The most that may be said is that the data are consistent with a cause of death common to the three types, and hence with the hypothesis that t^{h7} carries the t^6 lethal factor. Since this is a simpler hypothesis than the alternative one that t^{h7} carries a different lethal factor causing death at a similar time and also causing death of the t^6t^{h7} compound, it has been accepted. Since t^{h7} differed from the viable alleles in carrying the wildtype allele of tf its lethality was another point in agreement with the idea put forward in the earlier paper that t^6 carried a lethal factor close to the locus of tf , and linked with the wildtype allele.

(ii) Other properties of t^{h7}

Of the remaining properties of t^{h7} , male fertility could not be tested since the relevant genotypes t^6t^{h7} and $t^{h7}t^{h7}$ were lethal, leaving only male segregation ratio and crossover-suppression to be studied. Table 3 shows the results of these tests: male segregation ratio did not differ significantly from normal, whereas crossover-suppression was almost complete. The two recombinant offspring from the linkage tests with males were both shown to be carrying new mutant alleles (see below) and hence arose through crossing-over within the abnormal chromosome region.

The almost complete crossover-suppression by t^{h7} suggested that it possessed the whole or almost the whole of the abnormal chromosome region present in t^6 . Since its lethal properties were the same as those of t^6 , it seemed likely that the mutational change had been at the opposite, T -modifying, end of the abnormal region. One possibility was duplication of the T -modifying factor as a result of unequal sister-strand crossing-over. Evidence in favour of this was obtained from a

series of mutants derived from t^{h7} . These arose spontaneously either in linkage tests or in the progeny of matings made to maintain a stock

TABLE 3
The properties of the allele t^{h7}

Property	Test mating		Offspring		
	♀	♂	Short-tailed	Normal	Per cent. t^{h7}
Segregation ratio	++	Tt^{h7}	89	95	51.6
Recombination between T and tf	$Ttf/t^{h7} +$ $+tf/+tf$	$+tf/+tf$ $Ttf/t^{h7} +$	Non-crossover	Cross-over	Per cent. recombination
			246 227	0 2	0.0 0.8

of t^{h7} . By good fortune they were of various types and, as with t^6 , study of their properties assisted in the analysis of the properties of t^{h7} itself.

3. THE PROPERTIES OF MUTANTS DERIVED FROM t^{h7}

It has been mentioned above that two animals found as recombinants in linkage tests with t^{h7} were shown to carry mutant t -alleles

TABLE 4
The original animal and T -modifying effect of the alleles t^{h13} to t^{h16}

Allele	Original animal		Phenotype of Tt^{hz}
	Phenotype	Genotype	
t^{h13}	Short-tailed non-tufted	$T(t^{h13}) +/+tf$	Short-tailed
t^{h14}	Normal-tailed tufted	$+tf/t^{h14}tf$	Tailless
t^{h15}	Normal-tailed tufted	$Ttf/t^{h15}tf$	Normal-tailed
t^{h16}	Tailless non-tufted	$Ttf/t^{h16} +$	Tailless

(t^{h13} and t^{h14}), and a third crossover in a different cross gave t^{h15} . In addition, among the offspring of matings of $Ttf/t^{h7} + \times Ttf/t^{h7} +$, all expected to have normal or only slightly shortened tails, one tailless young was found.

Tables 4-7 show the results of tests of the various properties of the four mutants. The alleles t^{h13} and t^{h15} resembled the two complementary types of allele derived from t^6 by crossing-over in the abnormal

TABLE 5

The viabilities of various genotypes involving t^{h13} , t^{h14} and t^{h16}

Allele	Genotype under test	Cross	Offspring			Conclusion
			Short-tailed	Tailless	Normal-tailed	
t^{h13}	$t^6 t^{h13}$ $t^{h7} t^{h13}$	$T(t^{h13}) \times T t^6$ $T(t^{h13}) t^{h2} \times T t^{h7}$	14 0	0 28	27 33	LETHAL LETHAL
t^{h14}	$t^{h14} t^{h14}$ $t^6 t^{h14}$ $t^{h7} t^{h14}$	$T t^{h14} \times T t^{h14}$ $T t^{h14} \times T t^6$ $T t^{h14} \times T t^{h7}$	0 0 0	23 14 10	13 20 3	VIALE VIALE VIALE
t^{h16}	$t^{h16} t^{h16}$ $t^6 t^{h16}$	$T t^{h16} \times T t^{h16}$ $T t^{h16} \times T t^6$	0 0	66 82	0 2	LETHAL LETHAL

TABLE 6

Segregation ratio of $T:t$ in Tt males mated to $++^t$ females

Allele	T	t	Per cent t	χ^2 1:1
t^{h13}	72	77	51.7	0.17
t^{h14}	75	76	50.3	0.007
t^{h15}	123	30	19.6	56.5
t^{h16}	37	82	68.9	17.0

TABLE 7

Recombination between T and t in the presence of t^{h13} to t^{h16}

Sex of heterozygote	Allele	Offspring			Recombination per cent.
		Non-crossover	Crossover	Total	
Female	t^{h13}	212	19	231	8.23
	t^{h14}	97	9	106	8.49
	t^{h15}	43	6	49	12.24
	t^{h16}	119	1	120	0.83
Male	t^{h13}	184	7	191	3.66
	t^{h14}	102	7	109	6.42
	t^{h15}	108	4	112	3.57
	t^{h16}	179	0	179	0.00

region. t^{h13} carried the t^6 -lethal factor but had no T -modifying effect, while t^{h15} lacked the lethal factor and carried the T -modifying effect of its parent allele unchanged. Both permitted crossing-over between T and tf , and t^{h15} showed a low male segregation ratio, as did some similar alleles derived from t^6 .

FIG. 1.—Diagrammatic representation of the abnormal chromosome region present in t^{h7} and the alleles derived from it.

The two other alleles, t^{h14} and t^{h16} , both formed tailless compounds with T . The chromosome carrying t^{h14} also carried tf , whereas that carrying t^{h16} had $+tf$. As fig. 1 shows, if t^{h7} possessed a duplication of the T -modifying factor, then t^{h14} and t^{h16} must have arisen through crossing-over between the two halves of the duplication and were complementary types. t^{h16} would be expected to possess all the properties of t^6 , whereas t^{h14} should have only the T -modifying effect.

These expectations were entirely fulfilled. t^{h14} was viable and fertile both in compound with t^6 and when homozygous, and viable in compound with t^{h7} . It had a normal male segregation ratio, and gave normal recombination values between T and tf . On the other hand t^{h16} possessed all the properties of t^6 . It was lethal both in compound with t^6 and when homozygous, had a high male segregation ratio like t^6 , and suppressed crossing-over between T and tf almost completely, with the few recombinant offspring carrying mutant alleles. It was in fact indistinguishable from t^6 .

There were two further interesting properties of t^{h15} . The first concerned the phenotype of $t^{h7}t^{h15}$. If t^{h7} carried a duplication then $t^{h7}t^{h15}$ animals should carry it homozygously. Matings of $Ttf/t^{h7} \times Ttf/t^{h15}tf$ were made in order to find whether t^{h7}/t^{h15} was viable, and if so, whether it had any phenotypic abnormality. From these matings 9 out of 59 offspring had an abnormal gait, described as "drunken". The abnormality was first detected in the third week of life when the animals showed a stiff, shuffling gait. As they became older the stiffness and shuffling grew worse and were accompanied by a tendency to overbalance suddenly to one side. A coarse tremor developed. The disability prevented the animals from masticating the ordinary cubed diet, but they could be kept alive on wet-mash food for several months. One female so kept and paired with a normal male produced a litter of three young but failed to rear them; other females and males left paired with normal animals all failed to breed. Hence it has not been possible to ascertain the genotype of these "drunken" mice directly. However, since they have not been produced by any mating which would not give $t^{h7}t^{h15}$ it is deduced that they are of this genotype. There is then the question whether it was in fact homozygosity for the duplicated T -modifying factor which produced the effect. The compounds $t^{h7}t^{h14}$ and t^6t^{h15} were viable and with a normal gait. Since t^6t^{h15} is thought to differ from $t^{h7}t^{h15}$ only in the duplication of the T -modifying factor, then it must be either the duplication or some closely associated chromosomal change that is responsible.

The second interesting property of t^{h15} concerned the viability of $t^{h15}t^{h15}$ homozygotes. When it had already been shown that t^{h15} lacked the t^6 -lethal factor, and that $t^{h7}t^{h15}$ had an abnormal gait, matings were made which would produce $t^{h15}t^{h15}$, in the expectation that animals of this genotype would resemble $t^{h7}t^{h15}$. In fact, out of 42 offspring none had abnormal gait. Moreover, the $t^{h15}t^{h15}$ offspring from these crosses were expected to be tufted, and very few tufted offspring were found. This suggested that $t^{h15}t^{h15}$ was lethal, but this point is still being investigated and the question remains open.

4. COMPOUND ALLELES

The properties of the mutant alleles derived from t^6 and t^{h7} showed that t^6 carried a T -modifying factor and a lethal factor. The question then arose whether t^6 consisted only of these two factors or whether

it had another part or parts, for convenience referred to as a "middle-piece".

Two pieces of evidence pointed to there being indeed a "middle-piece". Firstly, the fact mentioned in the earlier paper that the ten viable crossover alleles derived from t^6 did not all have the same properties, but were of at least four types, suggested that some at least of them carried more of t^6 than merely the T -modifying factor. Secondly, heterozygotes carrying t^{h18} (and hence the lethal factor) and a viable allele (and hence the T -modifying factor) could easily be made, e.g. $T(t^{h18}) + /t^{h2}tf$, and in these animals crossing-over between T and tf was not suppressed, whereas if the whole length of t^6 were present one would expect complete crossover-suppression. However, in these $T(t^{h18}) + /t^{h2}tf$ heterozygotes, the two t -alleles were on the two

TABLE 8

Recombination between T and tf in the presence of compound t -alleles.

Heterozygote		Offspring			Recombination per cent.
Genotype	Sex	Non-crossover	Crossover	Total	
$Ttf/t^{h2}(t^{h18}) +$	♀	163	11	174	6.32
$Ttf/t^{h2}(t^{h18}) +$	♂	148	5	153	3.28
$Ttf/t^{h6}(t^{h18}) +$	♀	48	3	51	5.88
$Ttf/t^{h6}(t^{h18}) +$	♂	87	3	90	3.33
$Ttf/t^{h11}(t^{h18}) +$	♂	172	11	183	6.01

homologous chromosomes. There remained the possibility that two such alleles carried on the same chromosome would interact with each other through some kind of position effect and reconstitute the full properties of t^6 , including complete crossover-suppression. To test this point suitable heterozygotes, e.g. $Ttf/t^{h2}(t^{h18}) +$, were derived by crossing-over from the repulsion heterozygotes and used in linkage tests. Table 8 shows that three different viable alleles, t^{h2} , t^{h6} and t^{h11} , combined with t^{h18} , permitted crossing-over in both sexes. This meant that t^6 had not been reconstituted when the T -modifying factor and the lethal factor were placed on the same chromosome, and hence that t^6 must include in addition to these two factors, a "middle-piece".

5. DISCUSSION

The nature of t -alleles has been a puzzle since their first discovery. Dunn long ago put forward the idea that they might be due to some chromosome structural change such as inversion, and Dunn, Bennett and Beasley (1962) more recently suggested that a series either of non-overlapping inversions or of deficiencies would explain the observed properties.

In the present work various new facts have been brought out which throw light on this problem. The first was the clear demonstration that the lethal effect of t^6 was due to a factor located at some point on the chromosome at a distance from the T -locus. Reciprocal crosses were found, some with the T -modifying effect but no lethal effect and others with the lethal effect only. Moreover, the alleles of this latter group (t^{h13} and t^{h18}) carried the lethal effect but not the crossover-suppressing effect, showing that these two properties also were separable, and hence that any explanations of the nature of t -alleles ascribing the lethal and crossover-suppressing effects to the same cause were not tenable.

The second point was the finding of the allele t^{h7} , with an altered T -modifying effect, and the suggestion that this change was due to a duplication of the relevant region, with the consequent implication that this region was not an amorph. Unfortunately, the evidence that a duplication is present in t^{h7} is not complete, since cytological demonstration of a small duplication is not possible in the mouse with present techniques, but the genetic evidence is as good as could be obtained. First, there is the reversal of the observed effect, which can be explained by duplication of a gene with less than normal activity, and then there is the reversion of the postulated duplicated gene back to the single type of effect, giving the two types of allele (t^{h14} and t^{h16}) that would be expected to result from crossing-over between the halves of the duplication. In order to explain the observed T -modifying effects of the various alleles one then has to postulate that the tailless alleles carry an allele homologous to T which has a gene activity less than normal, and so enhances the effect of T , while in alleles such as t^{h7} two doses of the corresponding gene give a gene activity greater than normal, so suppressing the effect of T . This means that the activity of the T -homologous gene in tailless alleles is greater than one-half normal.

Yet a further point that emerged from the present study was that the T -modifying factor and the lethal factor do not constitute the whole of the abnormal region present in t^6 . This was brought out firstly by the viable alleles discussed in the previous paper, which differed among themselves in male segregation ratio and crossover-suppression, showing that some at least of them carried more of the abnormal region than just the T -modifying factor. Secondly, it was shown by the experiments in which the T -modifying and lethal factors were put together to make compound alleles which then did not show all the properties of t^6 , indicating that t^6 consisted of more than just these two factors. Moreover, some properties, in particular crossover-suppression and male segregation ratio, did not depend on specific factors but on the whole length of abnormal region. Male segregation ratio, for instance, could be changed by loss of the t^6 -lethal factor, by duplication of the T -modifying factor, and was affected by a "middle-piece" between these two factors.

These and other facts must be taken into account in formulating any hypothesis about the nature of *t*-alleles. The major choice is between a structural change such as inversion or deletion of a chromosome part, and a functional one such as a change to heterochromatin. Dunn, Bennett and Beasley, as mentioned above, favoured a structural change but the present evidence does not fit so well with this idea. It is not possible to explain the whole of the properties of *t*⁶ in terms of a deficiency, since the *T*-modifying factor behaves as though it is not an amorph. Similarly, an inversion leading to crossover-suppression cannot explain the whole of the properties, since either the *T*-modifying or the lethal effect may be present without crossover-suppression. Moreover, it is not easy to see how one lethal could by simple crossing-over give rise to a compensating one.

This leaves the possibility of a functional change in the chromosome, such as a change of state from euchromatin to heterochromatin, insertion of blocks of intercalary heterochromatin, and so on. This seems to provide the best explanation so far. It is postulated that in *t*⁶ there has been a functional change of the chromatin such as to cause a reduction in gene activity and to inhibit specific pairing. This latter effect is known to be a property of heterochromatin in *Drosophila* (Hannah, 1951). It would explain the crossover-suppression and also why the occasional rare crossovers might be unequal, resulting in duplication of a small part of the abnormal region. Alternatively, unequal crossing-over might result in deletion of a small part of the region and this could account for lethality. It could also explain how one lethal may by crossing-over give rise to a different, complementing, lethal, due to a deletion at a new point. There is also the possibility that the lethal actions of some alleles are due not to deletions but to position effects on particular gene loci due to the juxtaposition of heterochromatin. Again, crossing-over could give rise to new complementing lethals. Partial lethality and partial complementation could also be explained if the position effect tended to die out gradually along the chromosome.

Using this explanation of *t*-alleles as due to a functional change in the chromatin, different alleles found occurring naturally would be considered to have different lengths of abnormal region, with duplications or deficiencies at different points. *t*⁶ is known to occupy the whole or a large part of the region between the loci of *T* and *tf*. Its crossover-suppressing effect does not extend much beyond *tf* (Lyon and Phillips, 1959) but one cannot say whether the allele extends beyond the *T* locus because the methods of detecting mutants only pick up those which result from crossing-over between *T* and *tf* (and are therefore detectable either as crossovers or through loss of the lethal factor). Unfortunately, little is yet known about the lengths of other alleles. Differences between alleles in length might result in differences in mutability, if mutation in this case means crossing-over. Dunn, Bennett and Beasley investigated this point but found no statistically

significant differences in mutability, and hence no positive evidence. A further point to be expected is that mutation from one lethal allele to another would not occur equally in all directions; a long allele could mutate by simple crossing-over to a shorter one but not *vice versa*. Some evidence of this is to be found in Dunn, Bennett and Beasley's list of the origins of mutant alleles. The known lethal alleles

TABLE 9

Mutation from one lethal t-allele to another

(All information from Dunn, Bennett and Beasley's table 3, unless otherwise stated)

Allelic group	Mutation rate	Mutations to viables	Mutations to lethals		References and remarks
			Allele	Group	
t^{w5} . . .	0.00197	many	t^{w18} t^{w20} t^{w21} t^{w32}	t^{w18} t^{w1} t^{w1} t^{12}	Dunn (1962)
Original t^1	0.00318	many	t^4 t^9 t^{12}	t^{w18} t^{w18} t^{12}	$t^4 = t^9$ (Gluecksohn-Waelsch 1962) $t^9 = t^{w18}$ (Dunn 1962)
t^{w1} . . .	0.00094	many	t^{w30}	t^{w18}	Dunn (1962)
t^{12} . . .	0.0025	at least 4	t^{20*}		* Omitted from discussion because mutant allele lost.
t^0 . . .	0.0013	many	...	...	...
t^{w18} . . .	0.00059	at least 2	...	...	...

can be divided into six groups, such that members of one group complement the lethality of all the other groups, and table 9 shows the mutations that have been observed from one group to another. The alleles can indeed be arranged in a series from the "longest" to the "shortest", such that supposed long alleles mutate to shorter ones but short alleles do not mutate to longer. This makes t^{w18} the shortest lethal allele and corroboration of this is obtained from the fact that it has the lowest mutation rate of all the lethals and permits crossing-over between T and tf , *i.e.*, its abnormal region does not extend the whole distance between these two loci. Unfortunately, the mutation rates of the other alleles do not agree well with the idea of their ascending length; if the wild and the laboratory alleles are considered as separate series then the agreement is good, but not if all six groups

are considered as one series. Moreover, the total number of known mutations from one lethal to another is still too small for the fact of uni-directional mutation to be considered firmly established. Therefore, the arrangement of the lethal t -alleles as a series of increasing length in the order t^{w18} , t^0 , t^{12} , t^{w1} , t^1 , t^{w5} is put forward merely as a tentative suggestion, not an established point. Nothing has been learned about how t -alleles arose from normal chromatin in the first

FIG. 2.—Representation of the hypothesis concerning the nature of t -alleles. Normal chromosome—black; functionally changed region—hatched; deleted region—white.

place, but it is suggested that somehow lengths of functionally changed, possibly heterochromatic, chromosome have arisen, and that different alleles have different lengths of abnormal region, with, at specific points, lethal factors, possibly duplications or deficiencies which have resulted from unequal crossing-over (fig. 2). Further crossing-over may lead to a viable or to a new complementing lethal allele, according to whether or not a new deficiency is created.

6. SUMMARY

The mutant t -allele t^{h7} , derived from t^6 , suppresses the expression of the gene T rather than enhancing it as all previously known t -alleles had done. Study of the properties of t^{h7} itself and of some mutant

alleles derived from it led to the hypothesis that t^{h7} carried a duplication of the *T*-modifying factor present in t^6 . Discussion of the properties of all the alleles described in this and a previous paper then led to the further suggestion that the chromosomal abnormality present in *t*-alleles was a functional change in the chromatin, possibly a heterochromatic one, leading to reduction in gene activity and loss of specific pairing. Unequal crossing-over within the region might then lead in addition to small duplications or deficiencies. Different *t*-alleles would be of different lengths with duplications or deficiencies at different points.

7. REFERENCES

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