GENETIC ANALYSIS OF SEVEN NEWLY DISCOVERED MUTANT ALLELES AT LOCUS T IN THE HOUSE MOUSE[1]

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ONE of the eventual goals of genetical research is to elucidate the relationship between four unknown but discoverable characteristics of the genetic material. These might be listed as: 1) the type of change to which one genetic locus or area is subject (mutation); 2) the structural character of that locus or area; 3) the kinds of developmental processes that are affected by changes in that localized material; and 4) the role which a locus with such properties may play in adaptive responses to the environment and thereby its probability of incorporation in some future species or varietal genotype. If we were suddenly to gain an understanding of these relationships the genetical millenium would have arrived, and we should, as investigators, temporarily join the unemployed. But we know that such an event is not at hand, for precise knowledge of the relationship between these primary attributes is not likely to develop from the study of any one species or any single line of attack. The goal is too distant a one to give us the practical directions we need in charting our way among the detailed technical studies which form the indispensable raw material for synthesis. Yet if we bear in mind what the end is, we shall at least be influenced in our choice of means, and choose to follow up, in the more modest ways in which experimental studies must be circumscribed, those problems and materials which offer some hope of making progress in these four problems, which show signs even now of having a single direction.

It is probably some such thoughts which have encouraged us to persist over a period of years in the study of material which many people consider refractory and slow but which to us presents fascinating immediate problems and almost daily surprises on the way toward a more ambitious and distant goal. The house mouse, as bred in captivity for hundreds of years, is as everyone knows, good for breeding experiments. Four or five generations a year, if not equal to the daily or bimonthly generation period of other useful animals and

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[2] It would not have been possible for us to maintain the breeding operations and observations on which work of this sort depends without the devoted help of a number of students and assistants of whom we should especially like to thank RUTH SEGAL and SHIRLEY KAMELL.

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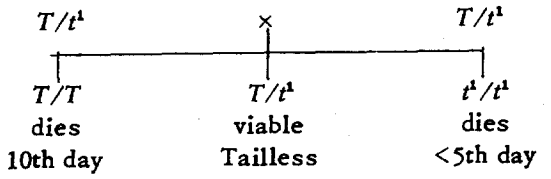
plants, is at least pretty good for an animal with warm blood which must suckle its young for three weeks and keep up a nearly continuous activity in confinement. We have always had great respect for one other quality of the mouse which underlies its usefulness for genetical research, its innate variability, which is of the same order as that which marks the animal toward which much mouse research is aimed, that is, man. But until we began to study one character, and particularly one area of one chromosome intensively, we had not realized how great is its potential variability. This character was simply tail length and form, in which the effects of some thirty-odd individual mutations have been observed, and of these more than half have been found to be concentrated in one small area of one chromosome.

The discovery of the first mutant in this area was made by DR. DOBROVOLSKAIA-ZAVADSKAIA in 1927, and she generously gave us not only stock of the original mutation, which was marked by a short tail, but of three other changes which turned out to be alleles of the first. Analysis of these alleles (CHESLEY and DUNN 1936; DUNN and GLUECKSOHN-SCHOENHEIMER 1939) led to the establishment of the balanced lethal system which is the key to the detection of further changes at this locus. We have been studying these changes both genetically and developmentally since 1936. KOBOZIEFF and POMRIASKINSKY-KOBOZIEFF (1939a and b) have independently reached the same interpretation concerning the first two mutations. In the present report we shall deal only with the genetically analyzed mutational changes found in one of the balanced lethal lines. This one has been called Line 29 and has been shown to breed true to taillessness in the manner shown below.

Tailless × Tailless



Actually we have observed at birth 3462 offspring from matings of $T/t^1 \times T/t^1$. Of these 3321 were regular (completely tailless) and 130 had short stumps or even short tails up to one-half of normal. Some of the latter have been tested and shown to be T/t^1; most of them are probably phenotypic variants of this genotype. But the remaining 11 had tails of normal length and these are probably valid exceptions. We succeeded in analyzing seven of these and each of these proved to have the genetic constitution t^1/t^n, t^n being a new allele at this locus. Of the four which could not be analyzed one died before testing, two were males which proved to be sterile, and one, a male, produced three small litters (he was probably quasi-sterile) of which the few descendants were lost in the F_2.

A conspectus of the seven which were analyzed in shown in table 1, together with the original mutation t^1 and a probable recurrence of it, t^2, found in

another balanced line (19). All of the t^n alleles agree in several important attributes. 1) All produce taillessness in compound with T and are recessive, in tail effect, in $+/t^n$. 2) All fail to show recombination with T or with t^1; this is the definition of their allelism. 3) Each new allele produces a normal-tailed compound t^1/t^n, although the viabilities of these compounds are not equal. This is the condition which permitted the detection of new changes. 4) All show normal disjunction in females T/t^n; while some males of each T/t^n compound show nonrandom segregation of T and t^n.

The alleles differ and several can be individually characterized by one or more of several properties. 1) Five are lethal when homozygous, and of these four can be distinguished by the stage and the manner in which the lethal effect occurs; while the fifth, not yet studied embryologically, differs from all the others in its extreme segregation ratio in male heterozygotes (see table 8).

TABLE 1

Some effects of seven new mutant alleles at locus T which produce taillessness in combination T/t^n, compared with those of the balanced line T/t^1 in which they arose.

Allele	Homozygote	Characters chiefly affected	Segregation ratio T/t^n ♂ $t^n : T$
T	Lethal 10th day	Notochord; allantois	1
t^1			
t^2	Lethal < 5th day	Preimplantation	> 1
t^4	Lethal 8th day	Early differentiation	< 1
t^9	Lethal 9th day	Early differentiation	< 1[1]
t^{12}	Lethal ?	Not studied	≫ 1
t^3	Viable	Normal	± 1
t^7	Viable	Normal	1
t^8	Viable	Normal	1
t^{11}	Viable	Normal	± 1

[1] 1 male out of 7 gave high ratio ($115t^9 : 49T$).

2) All of the t^n lethals, when in compound with T, in males, segregate in some ratio which departs from the normal 1 : 1 but in different directions in different lethals. Thus in T/t^1 and T/t^{12} males the t^1 and t^{12} sperm outnumber those with T, sometimes by wide margins, while in T/t^4 and T/t^9 the reverse is generally, but not uniformly the case ($T/+$ shows normal segregation). 3) The relative viabilities before birth of some of the compounds of lethal alleles are different, thus t^1/t^{12} has very low viability while t^1/t^4 and t^1/t^9 have much higher viabilities before birth. Variation in viability of compounds of the same alleles was found in the case of t^1/t^0 (t^0 occurred independently of t^1) and shows that factors at other loci are also involved in viability effects. In this case also characteristic abnormalities were found in some of the t^0/t^1 embryos (DUNN and GLUECKSOHN-SCHOENHEIMER 1943). Future work may reveal specific effects of t-alleles and of other factors in compounds.

The four viable alleles are not immediately distinguishable since all produce normal or nearly normal tails in the homozygotes, and the segregation ratios

TABLE 2

Tailless line 3 (T/t^3).

♀ Parents ♂		Normal	Brachy	Tailless
Tailless × tailless	$T/t^3 \times T/t^3$	197		474
Normal × tailless	$+/+ \times T/t^3$	343	401	1
Tailless × normal	$T/t^3 \times +/+$	71	72	1
Brachy × tailless	$T/+ \times T/t^3$	79	84	101
Normal × normal	$t^3/t^3 \times t^3t^3$	315		
Brachy × normal	$T/+ \times t^3/t^3$	154	4[1]	178
Normal[2] × Brachy	$t^1t^3 \times T/+$	273		213

[1]Phenotypic variants probably T/t^3.
[2]From cross of $T/t^3 \times T/t^1$.

of their male compounds T/t^n are not seriously disturbed. Yet even amongst the viable alleles there are indications of some individual differences. In most of the male compounds t^1/t^n which have been tested, fertility is either absent or impaired, but probably to different degrees in different combinations. Thus most t^1/t^3 males are sterile with a few quasi-sterile, while t^1/t^7 males have

TABLE 3

Tailless line 4.

♀ Parents ♂		Normal	Brachy	Tailless
Tailless × tailless	$T/t^4 \times T/t^4$			334
Normal × tailless	$+/+ \times T/t^4$	522	788	1*
Tailless × normal	$T/t^4 \times +/+$	166	156	
Brachy × F_1 normal	$T/+ \times +/t^4$	370	184	171
F_1 normal × Brachy	$+/t^4 \times T/+$	30	20	17

*Phenotypic variant of $T/+$.

higher fertilities (DUNN 1952). Before reliable distinctions of this sort amongst the viables can be made, the different stocks must be made otherwise isogenic and this has not yet been completed.

These judgments are of course tentative and preliminary. The breeding data on which they rest are set out in tables 2–8. The indications at present are that many of the changes found in the T/t^1 balanced stock, and analyzed, are new and different from others. It is as yet too soon to say whether all of the effects

TABLE 4

Tailless line 7.

♀ Parents ♂		Normal	Brachy	Tailless
Tailless × tailless	$T/t^7 \times T/t^7$	30		76
Normal × tailless	$+/+ \times T/t^7$	150	161	
Tailless × normal	$T/t^7 \times +/+$	22	21	
Brachy × tailless	$T/+ \times T/t^7$	120	117	126
F_1 normal × Brachy	$+/t^7 \times T/+$	51	26	24
Brachy × normal	$T/+ \times t^7/t^7$	34		32

TABLE 5

Tailless line 8.

♀ Parents ♂		Normal	Brachy	Tailless
Tailless × tailless	$T/t^8 \times T/t^8$	99	1*	202
Normal × tailless	$+/+ \times T/t^8$	166	167	3#
Tailless × normal	$T/t^8 \times +/+$	92	94	1
Brachy × tailless	$T/+ \times T/t^8$	59	45	36
Tailless × Brachy	$T/t^8 \times T/+$	28	37	28
Brachy × F_1 normal	$T/+ \times +/t^8$	38	9	16
F_1 normal × Brachy	$+/t^8 \times T/+$	66	29	25
Brachy × normal	$T/+ \times t^8t^8$	8		11
$t^8t^8 \times t^8t^8$		13		

*Phenotypic variant of t^8/t^8.
#One tested was phenotypic variant of $T/+$.

by which alleles appear to differ, such as segregation ratio and degree of male sterility in compounds, are properties peculiar to each allele rather than of the genetic background of the stocks in which they have been studied. But some distinctions, such as lethality and viability and the stage and manner of lethal action, are surely properties primarily of the individual alleles.

TABLE 6

Tailless line 9.

♀ Parents ♂		Normal	Brachy	Tailless
Tailless × tailless	$T/t^9 \times T/t^9$			175
Normal × tailless	$+/+ \times T/t^9$	184	212	
Tailless × normal	$T/t^9 \times +/+$	97	91	
Brachy × tailless	$T/+ \times T/t^9$	73	87	62
Tailless × Brachy	$T/t^9 \times T/+$	10	7	11
Brachy × F_1 normal	$T/+ \times +/t^9$	53	25	18
F_1 normal × Brachy	$+/t^9 \times T/+$	70	52	26

Assuming for the present that each exception found represents a different change in locus *T*, what can be said about the nature of the changes? Are they mutations in the broad sense of the word as meaning novel changes in a gene or chromosome, or are they, like many of the changes in Oenothera which were described as mutations, also as in the latter case rare recombinations due to

TABLE 7

Tailless line 11.

♀ Parents ♂		Normal	Brachy	Tailless
Tailless × tailless	$T/t^{11} \times T/t^{11}$	14		50
Brachy × tailless	$T/+ \times T/t^{11}$	41	49	64
Tailless × Brachy	$T/t^{11} \times T/+$	7	15	8
F_1 normal × Brachy	$+/t^{11} \times T/+$	18	7	8
Normal × tailless	$t^{11}/t^{11} \times T/t^{11}$	37		39
Brachy × normal	$T/+ \times t^{11}/t^{11}$	9		18

crossing over within the balanced lethal system? Categorical answers cannot be given but evidence at present rather favors the mutation hypothesis. The detectable results of crossing over in $T +/+ t^1$ for example should be wild type gametes ++ and these in combination with regular gametes T and t^1 should produce exceptions $T/+$ and $t^1/+$. These have never been detected. Ordinary recombination should produce repeatedly the same types of crossover gametes whereas each of the exceptions analyzed has proved to be different. GRÜNEBERG (1952) has suggested that since t^1 is probably an inversion, crossing over within it might give rise to duplications of some loci and deficiencies of others and thus the compounds of different lethal changes should be viable. Without nearby chromosome markers this hypothesis cannot be tested at present. It would require that some duplications and deficiencies should be viable since we have four viable alleles at the T locus. If it is an inversion it must be very short (JAFFE 1952); consequently crossing over within it should tend to produce short deficiencies or duplications which repeat themselves, that is, the same allele should arise repeatedly but not new inversions. We do not yet know whether the new lethal alleles like the older ones t^1 and t^0 give evidence of

TABLE 8

Tailless line 12.

♀ Parents ♂		Normal	Brachy	Tailless
Tailless × tailless	$T/t^{12} \times T/t^{12}$			94
Brachy × tailless	$T/+ \times T/t^{12}$	32	9	30
Normal × tailless	$+/+ \times T/t^{12}$	146	13	
F_1 normal × Brachy	$+/t^{12} \times T/+$	42	14	15
Tailless 29 × tailless 12	$T/t^1 \times T/t^{12}$	26		256
Tailless 12 × tailless 29	$T/t^{12} \times T/t^1$	10		150
F_1 normal × Brachy	$t^1t^{12} \times T/+$	62		45

being inversions by the suppression of crossing over (DUNN and CASPARI 1945). At least one of the new viable alleles (t^3) does take part in recombination in the *T-Ki* region (DUNN and GLUECKSOHN-WAELSCH, in press).

The frequency of these changes must be very high. The exact ratio is difficult to estimate. We have found a minimum of 7 and probably 11 changes within a few years and amongst only 3500 offspring observed from $T/t^1 \times T/t^1$. All of the exceptions tested had the composition t^1/t^n and several of these compounds have less than normal viability, so that some of them may die as embryos and escape detection.

Most of those detected occurred in related individuals of one family line of a Line 29 T/t^1 stock. The t^4 exception was found in the inbred descendants (four generations of brother-sister matings) of the pair which produced t^3. The original t^1/t^4 exception (a female) was mated to $T/+$ and both tailless (T/t^1 and T/t^4) and normal-tailed ($+/t^1$ and $+/t^4$) offspring were tested. One normal son crossed to $T/+$ had 13 tailless offspring which lived to be tested by T/t^1. The results of these tests are shown in table 9.

There is no doubt that the father of these 13 animals which bred like T/t^1 was himself $+/t^1$, but in the T/t^1 offspring (or in the T/t^1 animals by which

they were tested) three new *t*-alleles arose. The extensive number of test offspring observed was of course in part responsible for the result; but 3 new changes in 437 observations is a rate within this family line which must be higher than in the general population of T/t^1.

Similarly, the origins of t^{10}, t^{11}, and t^{12} are connected; t^{10} was found in the fifth brother-sister generation following a cross of T/t^1 to $T/+$. The mother of the t^1/t^{10} exception was mated to a brother of the exception, and the resulting group of a brother and his sisters produced 84 tailless and one normal which proved to be t^1/t^{11}. The same brother of the t^1/t^{10} exception was mated to his sister, and amongst the grandchildren of these one normal-tailed exception was found, and from a sibling of this t^{12} was isolated.

It is perhaps coincidence that the T/t^1 families in which the exceptions were found were the only ones which regularly produced the phenotypic variants of

TABLE 9

Tests of 13 tailless offspring from a cross of Brachy T/+ females by ♂ 19157 +/t^1, a son of the original mutant t^1/t^4.

Animal No.	Progeny from test cross with T/t^1	Diagnosis
1	33 tailless	T/t^1
2	37 tailless	T/t^1
3	44 tailless	T/t^1
4	99 tailless 1 normal (= t^1/t^8)	T/t^1
5	33 tailless	T/t^1
6	18 tailless	T/t^1
7	57 tailless	T/t^1
8	8 tailless 1 normal (= t^1/t^7)	T/t^1 ?
9	20 tailless	T/t^1
10	24 tailless	T/t^1
11	15 tailless 1 normal (= t^1/t^9)	T/t^1 ?
12	20 tailless	T/t^1
13	29 tailless	T/t^1
Total	437	

T/t^1 known as stump tails or short tails and also sometimes produced offspring with urogenital abnormality resembling those with the mutation *ur* which was first found in one of these lines.

These related occurrences suggest some sort of inherited instability or some chainwise connection as though the first change had touched off a succession of other ones. The connection in the seven cases analyzed however was always through t^1 since the new alleles did not arise from each other but always from T/t^1. Inbred lines of $T/+$ (Brachy) on the other hand which we have bred since 1930 appear to be stable. The occasional tailless animals found in these lines have always proved when tested to be $T/+$, that is, they are phenotypic modifications of the Brachy phenotype. This does not mean necessarily that the changes in the T/t^1 line occur in the t^1 chromosome. In the one viable allele tested for crossing over suppression, the chromosome with t^3 had lost the inversion, or at least the crossover suppressor associated with t^1. The changes may of course be induced in the T chromosome by the presence of t^1.

One fact of special interest was noted in two cases. Although the occurrence of a normal-tailed exception heralded the presence of a new allele in all cases, in t^3 and t^{12} the new tailless line was not obtained solely from the exception. In the case of t^3, reasons were given (DUNN and GLUECKSOHN-WAELSCH 1951) for assuming that the change occurred more than once in related individuals, and in at least one of these it probably occurred before the last meiotic division since several mutated gametes were recovered from an individual known to be T/t^1. This may have been the case also with t^{12}, for the exception, a male, was sterile and a new allele was recovered from two tailless siblings of the exception. Each of these proved to be T/t^{12} by giving normal-tailed offspring when tested by T/t^1 from the standard line. Two other sibs similarly tested gave 37 and 34 tailless offspring. It is not unlikely that in the mouse, mutation in premeiotic stages will prove to be less uncommon than in insects and that this is not peculiar to the T-locus but applies to some other loci as well (W. S. RUSSELL 1951).

There is no evidence that factors at other loci are responsible for the instability. Although t^3 appeared only one generation after an outcross of T/t^1, the other alleles occurred in descendants of five to eight generations of brother-by-sister matings so that introduction of other factors from outcrosses is probably not responsible.

Moreover, the presence of t^1 is not an essential condition for the instability since we have also found normal-tailed exceptions in the inbred balanced Line A, T/t^0, two in 1942 and two in 1952. None of these exceptions, due to poor viability and sterility, has given rise to lines which could be analyzed.

Finally, as shown recently (DUNN and MORGAN 1952), t-alleles have also been found in populations of wild mice from widely different localities.

This opens up a host of problems concerning the function of this locus in the wild which we hope can be studied by us and others interested. One great question is what permits t-alleles to be maintained, possibly above equilibrium values, in the wild. In addition to the factors of heterozygote advantage and mutation pressure which have been investigated in other materials, the first t-allele isolated from the wild segregates from heterozygotes in ratios far exceeding 1 : 1. Our first wild males $+/t^w$ produced about six t^w gametes for each + gamete. This may more than compensate for its homozygous lethal effect; and this may provide a clue to the persistence of lethal mutations and to the unusual segregation mechanism as of some adaptive significance.

Thus in spite of the high frequency with which such genetic changes arise, it seems most reasonable at present to treat them as "mutations," although "mutation" should not exclude the type of two-break changes which MULLER has called rearrangements. The large number of them detected in the T/t^1 lines, although it certainly implies high mutability, is also a reflection of the ease of detection and identification in such lines. The balanced lethal systems T/t^n, where t^n is a lethal, are as it were traps baited to catch mutants of this type; that is mutations to alleles which show fairly high viability in compound with the old allele. Mutants with low viability in compound will tend to escape this trap.

Those mutations from one viable allele to another cannot of course be detected by this balanced lethal method. We are testing another method for detecting these which may prove to be too cumbersome, that is, the different degrees of interaction in male compounds t^n/t^w in respect to sterility and quasi-sterility. We know for example that t^3 and t^7, both viable, show quite different interactions in this respect with t^1; t^1/t^3 males are sterile or nearly so; t^1/t^7 may have nearly normal fertility (DUNN 1952).

DISCUSSION

What now can be said, in the light of the data given above, about the general questions in the introduction? It is evident at the least that three of the primary characteristics of the genetic material can be identified and profitably studied at locus T in the mouse: the types of mutative change, the kinds of developmental processes they give rise to and the role of the locus in adaptive responses. Concerning these traits some evidence has been obtained and some suggestions about relations among them have emerged. The fourth trait, the structural character of the locus, is still unknown, and in the absence of the essential cytogenetic evidence no conclusive or adequate hypothesis relating the four traits can be formulated.

It is clear that the locus is quite mutable both in the balanced condition T/t^1 in which 11/3500 changes to t^n were noted, in T/t^0 (4/2000) and in wild populations, four out of five of which were found to contain $+/t^w$ individuals, t^w being any allele of T found in the wild. The likelihood that the changes found in T/t^1 populations are merely recombinations in balanced lines is reduced by finding that similar changes are common in wild populations. The mutability of the locus appears not to depend on any particular combination of alleles, or even upon the previous presence of a change at this locus, since distant populations contain diverse t^w alleles.

At least three different types of alleles have arisen as a result of these changes: (1) the dominant lethal type T recorded by DOBROVOLSKAIA (1927) and independently by CARTER and PHILLIPS (1950), and which also may have occurred in the stocks of DUBOSQ (1922); (2) recessive lethals such as t^0, t^1, t^4, t^9 and t^{12}; (3) recessive alleles such as t^3, t^7, t^8 and t^{11} which are viable and normal-tailed when homozygous. Each of the last two types has also been found in wild mice. Two of the lethals (t^0, t^1) prevent recombination in the immediate neighborhood of T, suggesting that they contain sectional changes, possibly inversions; while at least one viable allele, t^3, is not a crossover suppressor. All act as alleles with each other t^0/t^3, t^4/t^7, etc. It is probable then that both sectional changes and point mutations arise with some frequency in the same area but the relation of these changes to the physical conditions in the chromosome is unknown.

Concerning the kinds of developmental processes affected by these changes, we know a good deal more. As pointed out previously (GLUECKSOHN-WAELSCH 1951) " changes in most of the genetic factors in Chromosome IX (near locus T) lead to abnormalities of derivatives of the notochord-mesoderm material and to phenomena traceable to an absence of functioning or to abnor-

mal functioning of this same material." The specific deviations from normal development associated with the several types of change at locus T are closely related to each other and in one case to those at a neighboring locus.

In the case of T, both notochord and somites are abnormal from early stages and death occurs at about 11 days. In the homozygote t^0/t^0 which dies shortly after implantation (5th day) no mesodermal structures at all are formed; in the case of t^1 we know only that the homozygote does not reach the stage of implantation, but we do not know when or how the zygote dies. In t^4/t^4 the development of the archenteron, which in the mouse is involved in the formation of notochord-mesoderm, is disturbed. Preliminary studies of t^9 homozygotes which die at 8–9 days have revealed abnormalities involving duplications of parts of the neural system which indicate a relationship with the homozygote *Ki Ki*, a mutation at a nearby locus. Inductive phenomena traceable to abnormalities in function of notochord-mesoderm material could well be responsible for the duplications in t^9/t^9 embryos. The similarity in homozygous effect of *Ki* with t^9, which is allelic with T while *Ki* is not an allele of T, seems very significant. The fundamental effects of the lethal members of the t-series studied up to now (T, t^0, t^1, t^4, t^9) all fit the assumption that the region of chromosome IX in which they together with *Ki* are located plays an important part in the normal functioning of the notochord-mesoderm material. The embryological studies have shown very clearly that while all t-type mutations studied have a common focus, each lethal can be distinguished by its developmental effect from each other one (T, t^0, t^1, t^4, t^9) proving that each lethal has originated in a different mutative event. This locus or area, because of its effect on structures of primary developmental importance, must have an important adaptive role. Its mutability may be correlated with its high developmental activity, and both may be related to the kind of material of which this region is composed. Since mutants, many of them lethal, are retained in heterozygous form in wild populations, the locus in heterozygous condition may make some positive contribution to development and viability. We know also that changes at this locus affect the segregation ratio $T : t^n$ and $+ : t^n$ in spermatogenesis. The mechanism which provides for an excess of lethal-bearing sperm, for example, t^1 or t^{12}, may thus have a definite adaptive value.

In sum, although it can not now be specified in detail how the mutability, developmental processes, and adaptive role of this locus are related, we believe our work has shown them to be interdependent, and specific experiments can now be planned to elucidate the mechanism of interdependence.

SUMMARY

Evidence from breeding experiments is presented in summary form indicating the occurrence by mutation in the balanced lethal line T/t^1 of three new lethal alleles (t^4, t^9, t^{12}) and four alleles (t^3, t^7, t^8, t^{11}) which are viable in homozygous form; these seven were found in about 3500 offspring from $T/t^1 \times T/t^1$ observed at birth together with four additional exceptions which were lost before genetical analysis could be made. Comparison of the breeding

behavior of these and review of evidence on developmental studies led to conclusions that locus T is 1) highly mutable; 2) concerned (together with a neighboring locus Ki) in the functioning of the notochord-mesoderm in the early embryo; 3) connected with some adaptive function which leads to retention of *t*-mutants, even when lethal, in wild populations. Relations between these characteristics of the locus are discussed.

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