A GENETICAL STUDY OF THE MUTATION 'FUSED' IN THE HOUSE MOUSE, WITH EVIDENCE CONCERNING ITS ALLELISM WITH A SIMILAR MUTATION 'KINK'

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Introduction

The mutations which have been found at and near locus *T* in the mouse are of special interest since they combine apparent similarity in phenotypic effects with juxtaposition of the affected loci (Dunn & Caspari, 1945). A large number of mutations have been recognized within an area which is probably not more than four crossover units in length (Dunn & Gluecksohn-Waelsch, 1953*a*). Three of these have sharply dominant effects, most readily recognized by shortening of the tail and ankyloses of neighbouring vertebrae: *T* (Brachyury), *Ki* (Kink) and *Fu* (Fused). At least a dozen recessives which behave as alleles of *T* have been recognized both in laboratory and wild populations (Dunn & Morgan, 1953) by their interaction with *T* to produce taillessness in T/t^n. These show no interaction with *Ki* and *Fu*, although two of them, t^0 and t^1, suppress crossing-over between *T* and *Ki*, a distance of four units, and are hence probably sectional changes. A third allele, t^3, does not suppress crossing-over in this area (Dunn & Gluecksohn-Waelsch, 1953*b*).

Two groups of mutations are clearly apparent: those at locus *T* on the one hand and *Fu* and *Ki* on the other. The latter two appeared in preliminary evidence to be separated by about one unit of crossover distance (Dunn & Caspari, 1945). Evidence to be presented in this paper indicates that they are alleles. They are indistinguishable in their effects on the tail and are similar in other ways as well. About four crossover units were shown to separate *T* from *Ki* and *Fu* (Dunn & Caspari, 1945).

The genetics and development of *T*, of several of the *t*-alleles, and of *Ki* have been described in some detail (see Gluecksohn-Waelsch, 1951, for review). Fused, which has been under observation since 1937, has presented special difficulties in the preparation and maintenance of homozygous stocks, in the failure of the mutation to manifest itself in *Fu*/+ and even in *Fu*/*Fu* condition, and in other ways. These have now been overcome sufficiently to permit an analysis of Fused with respect to its transmission and expression, its allelism with *Ki*, and some judgement concerning the question whether a variety of *Fu* alleles exist amongst which recombination occurs.

Two of the chief peculiarities of Fused were pointed out when it was first described by Reed (1937). These were its frequent failure to express itself in heterozygotes *Fu*/+; and the tendency for this failure to occur more frequently when *Fu* was derived from a female heterozygote (*Fu*/+) than from a comparable male (*Fu*/+). The persistence of this difference in backcrosses of *Fu*/+ to the same normal stock led Reed to assume that modifying genes acted upon the egg before fertilization to inhibit the expression of *Fu*.

Reed also noted the pleiotropic effect of *Fu* on the skeleton, since in addition to the fused tail vertebrae from which the mutation was named fusions of adjacent ribs and bifurcation of the tail were also found in some Fused animals. Although he found some Fused homozygotes, the question of the viability and other peculiarities of the homozygotes was left open. Reed presented some data showing that *Fu* and *T* were linked and considered *Fu* (T^f in his terminology) as a less severe allele of *T*.

Our observations in general confirm those of Reed with respect to the dominance and pleiotropic effect of *Fu*, and add anaemia at birth and waltzing behaviour and deafness as additional expressions of *Fu* in some fused animals, while spina bifida aperta is occasionally found amongst newborn Fused. Several cases of kidneys missing or abnormal have also been found in Fused homozygotes, as well as sirenoid monsters (Gluecksohn-Schoenheimer & Dunn, 1945). We have found that *Fu/Fu* may be of normal viability in certain inbred lines.

The difference in the manifestation of *Fu* in heterozygotes derived from *Fu*/+ females as compared with those from *Fu*/+ males, which was one of the striking features which Reed described as characteristic of *Fu*, is not an invariable peculiarity of this mutation.

Data on the genetical analyses of Fused to support the above statements are presented below.

Table 1. *The distribution of* 235 F_2 *animals from the cross of one Fu/Fu male by two normal females of line CF*

F_1 Parents	Fused grades of F_2 progeny*								
	0[t]	1/8	1/4	1/2	3/4	7/8	sl.	Total fused	n
F_1 ♀ 11786 *Fu* 2/3 × 11789-90 *Fu* 3/4	1[a]	2	3	3	30	1	.	40	7
F_1 ♀ 11787 *Fu* 2/3 × 11789-90 *Fu* 3/4	.	1	6	1	24	5	.	37	15
F_1 ♀ 11788 *Fu* 3/4 × 11789-90 *Fu* 3/4	1[b]	2	.	1	28	10	.	42	9
F_1 ♀ 11791 *Fu* 3/4 × 11789-90 *Fu* 3/4	1[c]	.	2[c]	7	16	13	5	44	27
F_1 ♀ 11792 *Fu* 3/4 × 11789-90 *Fu* 3/4	.	.	1	1	10	.	.	12	2
Total F_2	3	5	12	13	108	29	5	175	60
F_2 animals tested and proved *Fu/Fu*	.	1	3	6	3	1	.	14	.
F_2 animals tested and proved *Fu*/+		.	.	.	23	1	.	24	.

* All progeny scored at birth. t = tailless. sl = slight Fused. n = normal.
[a] siren. [b] siren. [c] imperforate.

Genetical analysis of Fused

The original stock of Fused was obtained from Dr Reed in 1935.* We crossed the original Fused animals with several different inbred normal lines in our laboratory preparatory to deriving inbred stocks homozygous for *Fu*. In these crosses *Fu* behaved as a good dominant.

Since it was probable that different stocks have different modifiers of Fused, we crossed one tested homozygous Fused male with two females from a long inbred normal stock (CF, originating from Carworth Farms Swiss) which had shown no tail abnormalities in our laboratory. The fourteen F_1 offspring were all Fused with tails about three-fourths the length of normal. Of these, two males and five females, full siblings, were mated to produce the F_2 shown in Table 1. The ratio of Fused to normal (175:60) was about that

* We are indebted to Dr Reed not only for the stock but for correspondence which indicates that both the anaemia and waltzing behaviour had been present in his Fused stock before it was sent to us, although he was not certain at that time of their association with *Fu*.

expected (176·25:58·75) indicating normal segregation and expression of *Fu*, although the proportions from different females varied rather widely.

The same F_1 animals were test-crossed with normals from the CF line with the results shown in Table 2. Here, too, the results showed normal segregation and expression in the offspring of reciprocal crosses.

A large sample of F_2 Fused animals was test-crossed by normal CF mates with the results shown in Table 3. Of 38 F_2 Fused which gave progenies of 10 or more, 13 proved

Table 2. *Results of backcrossing F_1 Fused by normals of line CF*

F_1 Parent	*Fu*	n	Total
F_1 ♀ 11786	9	16	25
F_1 ♀ 11787	3	2	5
F_1 ♀ 11788	3	4	7
F_1 ♀ 11791	14	13	27
All ♀♀	29	35	64
F_1 ♂ 11789	61	52	113
F_1 ♂ 11790	44	48	92
All ♂♂	105	100	205

Table 3. *Tests of F_2 animals from (Fused × normal (CF)) by normal (CF)*

Fu/Fu				*Fu/+*				*Fu/+*				+/+ !			
F_2 ♀♀	tail	*Fu*	n	F_2 ♀♀	tail	*Fu*	n	F_2 ♂♂	tail	*Fu*	n	F_2 ♀♀	tail	*Fu*	n
12067	2/3	18	1	11912	2/3	8	7	11873	2/3	10	6	11866	7/8	.	11
12205	1/8	10	.	12023	2/3	2	8	11874	?	11	16	4 *Fu* ♀♀[e]		.	18
12228	1/3	16	1	12106	3/4	8	4	12230	2/3	11	14				
12367	1/2	10	.	12118	?	2	8	12498	2/3	5	12				
12370	7/8	14	.	12206	3/4	7	8	12572	3/4	10	7				
12387	1/3	12	3[a]	12502	2/3	8	5	12694	2/3	6	7				
12569	1/3	15	1[a]	12503	2/3	5	5	12772	2/3	12	12				
12496	1/2	24	5[b]	12662	3/4	15	15	12845	2/3	6	5				
				12664	7/8	9	7	12846	3/4	9	9				
8 *Fu/Fu* ♀♀		119	11	12693	2/3	11	11	12888	2/3[f]	65	57				
F_2 ♂♂	tail	*Fu*	n	12742	2/3	15[c]	11	12504[g]	2/3	88	77[h]				
12190	1/2	22	.	12884	3/4	9	16	11 *Fu/+* ♂♂		233	222				
12191	1/2	13	.	12885	2/3	9	9	12 F_2 *Fu/+* ♂♂[e]		31	47				
12661	1/2	23	.	12886	3/4	6	5								
12744	2/3	38	4	14 *Fu/+* ♀♀		113	119								
12208	3/4	10	.	Doubtful											
5 *Fu/Fu* ♂♂		106	4	♀♀	tail	*Fu*	n								
				12120	3/4	30	15[d]								
				21 F_2 *Fu/+* ♀♀[e]		74	99								

[a] Abnormal tail tip or slight Fused. [b] Birth record: 21 Fused: 8 normal. [c] One tailless imperforate with fused kidneys, no bladder, gut ending at caecum. [d] Five normal offspring tested: 4 = +/+; 1 = *Fu/+*. [e] With less than 10 offspring. [f] First 7 litters = 37 *Fu*: 23 n; last 6 litters = 28 *Fu*: 34 n. [g] First 9 litters = 47 *Fu*: 25 n; last 9 litters = 41 *Fu*: 46 n. [h] Six normal offspring tested = +/+.

to be *Fu/Fu*, while 25 were diagnosed as *Fu/+*. This is close to the 1:2 ratio expected, and again indicates normal segregation. If we consider only progenies of 10 or more then the results of reciprocal test crosses are as shown in Table 4. There is no indication of difference in the reciprocal test crosses.

The data from incompletely tested F_2 animals show some excess of normals, but this occurs in both reciprocal test crosses. The meaning of this is not clear unless first litters are likely to contain more normal overlaps, and some preliminary studies indicate that this is unlikely.

More troublesome is the case of one F_2 *Fu* female which gave 30 *Fu* and 15 normal offspring. If she was *Fu/Fu* then all of her normal offspring should be *Fu*/+, but on testing by CF normals one turned out to be *Fu*/+, while four of them gave no Fused in progenies of ten or more. Later experience showed that the latter test does not exclude the possibility that some were *Fu*/+. The most likely explanation is that she was *Fu/Fu* but transmitted also something which suppressed the expression of *Fu*. One female, phenotypically Fused, gave 11 normal offspring. Since these were not tested it is not known whether she was *Fu*/+ or +/+ with either an injured tail or another Fused-like recessive mutation.

Table 4. *Test crosses of F_2 Fu/Fu and Fu/+ by + + (CF)*

	Fu	n
5 ♂♂ *Fu/Fu*	106	4
8 ♀♀ *Fu/Fu*	119	11*
11 ♂♂ *Fu*/+	233	222
14 ♀♀ *Fu*/+	113	119

* 4 slight *Fu* or abnormal tail tip.

Table 5. *Effects of inbreeding and selection on the tail length of Fused homozygotes*

		Tail length of offspring (at birth)										
Family	Generation	0[a]	1/8	1/4	1/3	1/2	2/3	3/4	7/8	sl.	Total *Fu*	n
	F_3 *a*	.	.	2	1	3[a]	7	5	1	.	19	1
	F_3 *b*	2[b]	11[b]	5	3	6	9	2	3	.	41	.
	F_3 *c*	2	1	.	1	3	6	5	.	.	18	.
a	F_4–F_{11}	11	43	36[c]	36	52	49	29	7	4	267	3[d]
a_1	F_4	.	5[h]	2	.	2	2	4	1	.	16	.
a_2	F_5–F_7	3	9[h]	14	14	29	36	19	9	2	135	3[e]
a_3	F_5–F_7	3	11	14	15	18	27	15	1	.	104	1[e]
a_4	F_6–F_7	1	9	5	6	4	2	8	1	.	36	.
a_5	F_7–F_8	1	4	3	.	5	3	3	2	1	22	1[e]
a_6	F_7–F_9	4	14[f]	6	9	30	28	21	3	3	118	.
a_7	F_8–F_{10}	3	20	9	7[g]	18	25	12	4	1	99	1
a_8	F_9–F_{10}	3	8[h]	14	13	16	22	10	2	2	90	1
		33	135	110	105	186	216	133	34	13	965	11
Short selection a_4, a_5, a_6, a_7, a_8		12	55	37	35	73	80	54	12	7	522	3
Long selection a, a_1, a_2, a_3		17	68	60	65	101	114	67	18	6	365	7

[a] 1 imperforate. [b] 3 imperforate. [c] 1 imperforate; 1 luxate. [d] 3 normal = *Fu/Fu*. [e] 1 normal = *Fu/Fu*. 1 normal = *Fu/Fu*. [f] 1 luxate; 1 spina bifida. [g] 1 imperforate. [h] 1 luxate.

This experiment thus proves that although *Fu* segregates normally as a simple dominant from crosses with the CF line, it occasionally fails to manifest itself in heterozygotes.

Expression of homozygous fused

Three brother-sister pairs of F_2 tested Fused homozygotes were mated to produce the F_3 generations shown in Table 5. Two of these, F_3a and F_3b, appeared to differ somewhat in average tail length, and consequently selection experiments were begun for long tails from F_3a and for short tails from F_3b. The short selection line was lost in the first generation due to abnormalities such as the imperforate syndrome (Dunn & Gluecksohn-Schoenheimer, 1944), poor viability and infertility in the tailless and shortest tailed offspring. The long selected line was continued as family *a* by mating in each generation a single male of tail length 2/3 or longer with a group of similar sisters or (in a few cases)

half-sisters. Results are shown as a F_4–F_{11} in Table 5. No significant change occurred in range or average tail length. Further selections were made from this line by mating brothers and sisters with short tails (1/2 or less) as families $a_{4,5,6,7,8}$, while further long selections (2/3 or longer) were made as families $a_{1,2,3}$. No significant changes followed either set of selections. In the total 'short-selected' the percentage frequency of the two most reliable tail-length categories (tailless and 7/8) are identical with those in the total 'long-selected', about 3·2% in each extreme category.

The wide range of variation shown in all generations of homozygous Fused has persisted through 14 additional generations of brother-sister matings. Now (F_{25}) the stock still produces occasional tailless and normal or nearly normal-tailed animals, and these extremes may occur within the same litter.

Of the 11 normal-tailed exceptions born in the homozygous Fused lines (Table 5) six were test-crossed by normals and all proved to be homozygous *Fu/Fu*. Hence they are phenotypic overlaps and do not indicate recombination between different Fused alleles. The latter possibility was tested further by mating 24 Fused homozygotes (from F_3–F_7) by normal. The test crosses gave 414 Fused and 28 normal. Nineteen of the normals were thoroughly tested by crossing again to normal and each one produced Fused offspring. If any of the normal exceptions had arisen from recombination within the Fused locus, they should fail to transmit a Fused allele. None proved to be recombinants; all were *Fu*/+ which failed to manifest *Fu* (normal overlaps).

The normal-tailed exceptions from *Fu/Fu* stock produced when tested by normal only 4 normal out of 84 (4·7%), while Fused siblings of the exceptions tested by the same normal stock produced 24 normal out of 358 (6·7%); that is, the exceptions which failed to manifest *Fu* produced no more overlaps than did the homozygotes which showed *Fu*. Hence suppression of *Fu*, if transmitted at all, is not due to dominant genes. Test crosses of *Fu/Fu* females yielded a somewhat higher proportion of normal overlaps (14/123) than did *Fu/Fu* males (14/319).

FURTHER TEST FOR ADDITIONAL ALLELES AT THE FUSED LOCUS

The persistence of great variability in tail length within the inbred lines of Fused suggested that either there were non-genetic factors acting or that there were several alleles of Fused with differing effects and that heterozygotes (compounds) of these had been selected for in the inbred lines. The first hypothesis has not been systematically tested, although a tabulation of tail length in successive litters from the same mother did not reveal any striking association with age of mother or ordinal number of litter.

An attempt to test the second hypothesis was made in the following way: Fused homozygotes from F_5–F_9 of the inbred lines were outcrossed to an inbred stock of Swiss origin (CFW) obtained from Carworth Farms. The F_1 Fused (*Fu*/+) animals while variable were mostly in the 3/4 and 7/8 tail classes. Several of these were again backcrossed to CFW normal and the process repeated through five backcrosses in an effort to increase the isogenicity of the *Fu* with the CFW stock. Subsequently *Fu*/+ animals from the backcross stock were mated together and several new inbred lines begun. The object was to permit different alleles of *Fu*, if present, to segregate out into the different lines derived from the backcrosses. The early generations of this new inbreeding experiment appeared to be repeating the experience, with respect to range and lack of difference between the lines, of the first experiment, and it was abandoned after F_4. The main

object of testing for *Fu* alleles was not accomplished; the prospects of getting a positive result were judged to be poor.

Allelism of fused and kink

Although Fused and Kink are extremely similar, they produced, in preliminary experiments, some apparent recombinants (Dunn & Caspari, 1945). With the stocks used at this laboratory we found no recombinants, the two normal exceptions from *Fu/Ki* proved to be *Fu/+* overlaps. A repetition with similar stocks led to the same result, i.e. no proved

Table 6. *Recombination tests of Fu/Ki × +/+*

	Test progeny		
		Normal	
Fu/Ki ♂♂	*Fu* or *Ki*	Tested *Fu/+*	Not tested
28062	202	11	1
28170	197	3	3
28172	166	9	3
28246	145	6	3
28609	54	3	1
28611	92	4	1
Fu/Ki ♀♀			
28171	45	2	.
28064	32	.	2
	933	38	14

Table 7. *Tests (× +/+) of normal-tailed exceptions from Table* 6

		Test progeny	
Fu/Ki parent	F_1 normal	Normal	*Fu* or *Ki*
♂ 28062	8 ♂♂	62	35
	3 ♀♀	25	15
28170	2 ♂♂	8	11
	1 ♀	33	4
28172	4 ♂♂	45	25
	5 ♀♀	35	12
28246	4 ♂♂	25	15
	2 ♀♀	28	4
28609	3 ♂♂	10	12
28611	3 ♂♂	29	23
	1 ♀	15	2
♀ 28171	2 ♀♀	22*	1
Total from 24 ♂♂		179	121
Total from 14 ♀♀		158	38

* F_1 ♀ gave 15 normal; one of these normals was tested and shown to be *Fu/+*; gave 5 normal 4 Fused.

recombinants. Finally, it was decided to retest the recombination hypothesis using adequate numbers and testing as many exceptions as possible. The test was made by crossing *Fu/Fu* (from F_{22-23}) × *Ki/+* and selecting as *Fu/Ki* those which gave, when tested by +/+, all or nearly all offspring showing either *Fu* or *Ki*. Eight *Fu/Ki* (6 males, 2 females) were found and tested extensively by mating with normals (Bagg albinos). The results are shown in Table 6. Each *Fu/Ki* produced a few exceptional normal-tailed animals, altogether 52 out of a total of 985. Whether these were recombinants (+/+) or normal overlaps (*Fu/+* or *Ki/+*) was tested by mating each exception with normal (Bagg albino). All 38 which were tested proved to be *Fu/+* or *Ki/+* by producing at least one *Fu* or *Ki* offspring (Table 7). Those not tested were probably a random sample of the

exceptions, some of which had been discarded before it was shown that the parent was *Fu/Ki*, and others died before they could be tested. Those which proved to be overlaps gave fewer *Fu* (or *Ki*) than normal offspring, indicating that more overlaps were produced by F_1 exceptions. There was a marked difference in this respect between male and female exceptions. The females produced 158 normal and 38 *Fu* (or *Ki*). All 14 females were proved to be *Fu*/+ or *Ki*/+; 13 of them produced in test crosses at least one *Fu* or *Ki* offspring; one of them produced 15 normal offspring only. These last offspring were again tested. One of them produced 5 normal and 4 *Fu*, proving him and hence his mother to be *Fu*/+. The failure of *Fu* to manifest itself in heterozygotes was noted by Reed (1937) in the first description of Fused, as was the greater frequency of normal overlaps from *Fu*/+ females than from *Fu*/+ males. These difficulties have prevented until now a decisive test of the allelism of *Fu* and *Ki*, but the present data give no evidence of recombination and make it highly probable that *Fu* and *Ki* are in fact alleles. To test the hypothesis of recombination let M be the expected number of recombinants out of N and R be the probability that none would be observed. Then with $R = e^{-M}$ and $N = 971$ (the number of backcross individuals shown not to contain a recombinant), $p \leqslant 0{\cdot}003$ with 95% confidence coefficient. We may therefore accept the hypothesis of no recombination and in practice treat *Fu* and *Ki* as alleles, referring to *Ki* hereafter as Fu^{Ki}.

This conclusion agrees well with the known phenotypic effects of these two mutations, which as heterozygotes are extremely similar. Both produce ankyloses between neighbouring vertebrae, occasional doubling or branching of the tail (forked tails); both produce, in certain combinations and in certain inbred lines, the circus movements, chorea and deafness associated in the waltzing syndrome. Their chief difference is that *Ki* is always lethal when homozygous, while *Fu*, under comparable conditions, is viable. In the stocks in which we have observed them the penetrance of *Ki* is higher, nearly all heterozygotes showing the *Ki* effect on the tail; while *Fu*/+ often shows a normal tail and occasionally *Fu/Fu* may be normal also. We have not made a special study of interaction in the compounds Fu/Fu^{Ki}. Of the eight animals proved to be of this genotype in our tests the tail length was 2/3 of normal in one, 1/2 in five, and 1/4 in two, while three of these showed the waltzing effect. Tail length in these is probably shorter than in *Ki*/+ but not shorter than in *Fu/Fu*. However, the effects of both mutations are so variable even in long inbred stock that an extensive study of these combinations in an otherwise isogenic stock would be necessary before comparisons could be made.

DISCUSSION

Several questions of genetical interest concerning the Fused mutation and its relation to similar nearby mutations have been answered. Fused is in general a normally transmitted dominant which, at least in several of the stocks in which we have maintained it, is viable when homozygous. Its expression, even in long inbred stocks, is quite variable, homozygotes usually having thickened, kinky tails, although they vary from no tail at all to tails of normal length and without kinks. The causes of this variability are unknown but are probably not genic. Other abnormalities (spina bifida, imperforate anus, abnormal kidneys, sirenoid malformations) are found occasionally in newborns and there is evidence of brain abnormalities (pseudencephaly) in some embryos (Gluecksohn-Waelsch, 1951). In certain combinations *Fu*/+ and *Fu/Fu* are accompanied by waltzing

behaviour and deafness. This does not appear at all in our present inbred *Fu*/*Fu* lines although it may appear in F_1 animals from crosses between Fused and normal. This connexion remains to be worked out.

In many of these peculiarities Fused resembles the mutation Kink, and it is not surprising to find that these are probably alleles. It is of course impossible to exclude, with the present evidence, recombination fractions as small as those found, e.g. 0·005, between pseudo-alleles at such loci as lozenge (Green & Green, 1949) or Star (Lewis, 1950) in *Drosophila*, and so we may accept *Fu* and Fu^{Ki} as alleles 'or closely linked pseudo-alleles with nearly identical phenotypes', and in practice this will mean 'alleles' in the broad sense. This has the effect of reducing from three to two the number of neighbouring loci with similar effects in linkage group IX and consequently makes it less unlikely that the association of *T* and *Fu* loci is due to chance.

There remains a certain resemblance between the abnormalities, especially the double formations, found in Fu^{Ki}/Fu^{Ki} embryos with those found in embryos of the same stage from one of the *t*-alleles (t^9/t^9) (Dunn & Gluecksohn-Waelsch, 1953*a*; Gluecksohn-Waelsch, 1953). Whether this indicates a control of this region of chromosome IX over early embryonic induction processes or a common response of embryos at that stage to abnormal processes remains to be seen.

It is also unknown whether the *Fu* locus resembles in its mutability the neighbouring *T* locus at which at least a dozen alleles have been recorded. Only two alleles of *Fu* can be identified with certainty, viz. *Fu* and Fu^{Ki}. Attempts to identify others in variable stocks of *Fu*/*Fu* have not been successful, but, on the other hand, not decisive. It is clear that the normal-tailed exceptions so far found in stocks of *Fu*/*Fu* and tested do not represent recombination between *Fu* alleles nor mutations. There is thus at present no evidence that *Fu* is a complex locus in the sense that *T* is. On the other hand, special methods for detecting changes, such as the balanced lethal systems of locus *T*, are not available at locus *Fu*.

One feature of *Fu* appears to be without parallel in the mutations of the IX linkage group, or for that matter in other mouse mutations. This is the tendency, which Reed found, for the offspring of *Fu*/+ females to fail to manifest *Fu* with much greater frequency than the offspring of *Fu*/+ males. Our evidence does not cast much additional light on this question, but the fact that in our tests of F_2 *Fu*/+ animals by normal, the ratio of Fused to normal was nearly the same from *Fu*/+ males and from *Fu*/+ females (Table 4) indicates that factors other than *Fu* may play a part in cases such as Reed found. That the 'Reed effect' occurs in our material under certain conditions is shown by the different ratios of *Fu* to normal produced by normal (*Fu*/+ or *Ki*/+) females (38:158) as compared with normal (*Fu*/+ or *Ki*/+) males (121:179) in our test crosses of normal exceptions from *Fu*/*Ki* (Table 8). It is probable that most or all of these exceptions were *Fu*/+ overlaps since *Ki*/+ nearly always manifests itself and no indication of the Reed effect has been noted in our work with *Ki*. This effect appears to be a part of the low penetrance of *Fu* in certain stocks, hence a response of *Fu* to a particular genotypic environment. Since *Fu* influences the development of the vertebrae in the embryo, it is not surprising that the genotypic environment acts through the mother to modify the expression of *Fu*. Our experiments do not contribute to an understanding of the mechanism of the effect.

SUMMARY

The mutation Fused, which produces shortening and thickening of the tail, together with ankyloses of contiguous vertebrae and other abnormalities, has been studied for twenty-five generations in inbred homozygous lines and in crosses. The homozygotes show a variable expression from taillessness (in 3·4 %) to normal tail (in 1·1 %), which was not changed by inbreeding or selection. The normal overlaps proved to be *Fu/Fu*, hence not recombinations. In outcrosses to normal it segregated normally as a dominant.

When crossed with the similar mutant Kink (*Ki*) the combination *Fu/Ki* has a shorter tail than *Fu/+*. *Fu/Ki* × + + gave 933 *Fu* or *Ki* and 52 normal. All of the latter which were tested proved to be *Fu/+* (or *Ki/+*), and the probability of recombination between *Fu/Ki* was shown to be $p \leqslant 0{\cdot}003$ with 95 % confidence coefficient. Hence *Fu* and Fu^{Ki} are assumed to be alleles.

The bearing of these facts on the constitution of the ninth linkage group which contains two sets of alleles $T \ldots t^n$ and $Fu \ldots Fu^{Ki}$ with similar effects is discussed.

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