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Linkage relations and some pleiotropic effects of the dreher mutant of the house mouse

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The mutant *dreher*, *dr*, of the mouse *Mus musculus* L. was first reported by Falconer & Sierts-Roth (1951). They described the circling behaviour of the affected animals and showed that the character was due to a recessive gene, not allelic with *v*, *sh*-1, *sh*-2, *je*, *kr*, *pi* or *fi* and not closely linked with W^v. Subsequently, Fischer (1956) described the morphological defects of the inner ear which are the basis of the dancing behaviour, and analysed their embryology (Fischer, 1958), while Bierwolf (1958) studied the accompanying defects of the brain.

The present paper describes the linkage relations of dreher and some previously unknown pleiotropic effects.

LINKAGE TESTS

Dreher homozygotes, from a stock kindly supplied by Dr D. S. Falconer, were crossed with animals from various linkage-testing stocks. To test linkage with recessive markers the F_1 animals were intercrossed, and in the case of dominant markers they were backcrossed to homozygous *drdr*. The results are shown in Tables 1 and 2. The original tests indicated possible loose linkages with *Re*, *T* and

Table 1. *Linkage tests of dreher with dominant markers* (M)

Marker	Heterozygote type	Offspring					χ^2	Recombination (%)
		M+	++	*Mdr*	+*dr*	Total		
Ca	C	52	45	46	55	198	1·29	46·0 ± 3·5
Mi^{wh}	C	54	44	51	49	198	0·32	48·0 ± 3·6
Ra	C	30	29	43	31	133	0·91	54·1 ± 4·3
Re	C	60	42	46	53	201	3·11	43·8 ± 3·5
	R	34	32	26	17	109	0·45	46·8 ± 4·8
Sd	C	21	40	7	28	96	0·04	49·0 ± 5·1
T	C	29	57	47	39	172	7·53	60·5 ± 3·7
	R	43	59	52	46	200	2·42	44·5 ± 3·5
W^v	C	39	56	46	47	188	1·36	54·3 ± 3·6

C = coupling; R = repulsion.

ln. The linkages with *Re* and *T* were not confirmed when the tests were repeated using repulsion heterozygotes. The linkage with leaden (*ln*) in linkage group XIII,

Table 2. *Linkage tests of dreher with recessive markers* (m)

Marker	Offspring ++	+m	dr+	drm	Total	χ^2	Recombination (%)
a	19	3	8	—	30	0·73	38·3 ± 13·7
b	95	31	19	13	158	2·70	59·8 ± 6·0
c^{ch}	86	40	19	13	158	0·48	54·1 ± 6·0
d	103	23	22	10	158	2·36	59·2 ± 6·0
fz	203	55	55	10	323	0·47	47·1 ± 4·2
ln	185	73	57	8	323	6·08	39·7 ± 4·2
p	66	24	16	5	111	0·08	48·0 ± 7·1
s	101	25	27	5	158	0·07	48·4 ± 6·0
vt	68	22	15	6	111	0·12	52·5 ± 7·1
wa − 2	68	22	17	4	111	0·17	47·1 ± 7·1

All heterozygotes were of the repulsion type. Recombination values and χ^2's were calculated by the method of Fisher (1946).

however, was confirmed by a test with dominant hemimelia, *Dh*, which Carter (1957) reported to be linked to *ln* with a recombination value of about 6%, the order of genes being *Dh–ln–fz*.

Threepoint backcrosses were made using heterozygotes of the type *dr* + +/+ *Dh ln* (Table 3). In these crosses dreher showed 27·2 ± 3·0% recombination with *Dh* and 27·7 ± 3·0% with *ln*. Two possible orders of the three genes which

Table 3. *Data obtained from threepoint backcrosses of the type* dr + +/+ Dh ln × dr + ln/dr + ln. *The data from female and male heterozygotes are shown separately*

Phenotype of progeny	No. of young from ♀ heterozygote	♂ heterozygote	
dr + +	70	5	Non-crossovers
+ *Dh ln*	71	7	153
+ + +	32	0	*dr* crossovers
dr Dh ln	20	3	55
dr + *ln*	3	0	*ln* crossovers
+ *Dh* +	2	0	5
dr Dh +	0	0	Double crossovers
+ + *ln*	4	0	4

would be compatible with these figures are *Dh–ln–dr* and *dr–Dh–ln*, the latter being the more probable. The first of these is ruled out since it would entail close linkage of *dr* with *fz*, which was not found. If the second order is accepted, then animals of the phenotype + + *ln* represent double crossovers, and it is surprising that four of these should have been found when the two intervals, *dr–Dh* and *Dh–ln*, are quite short. However, Searle (1959) found that occasional *Dh* heterozygotes have

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completely normal limbs, and since in this experiment *Dh* was classified by limb abnormality only, it is possible that these four animals were *Dh*+ normal overlaps. If so, their genotype was $+Dh\ ln/dr\ +ln$ and they were non-crossovers. No double crossovers of the complementary type were found; there is thus no bar to accepting the second order, *dr–Dh–ln*, and it will be considered to be established. This means that *dr* is close to *Lp* and to the translocation break in T190, but its position in relation to these is not known. Normal overlapping by *Dh* will tend to increase the apparent recombination between it and *dr*, and a more accurate value for the recombination fraction will be obtained by considering only the manifest *Dh* young. In the backcross experiment there were 103 *Dh* young, of which 23 were also dreher and therefore crossovers. This gives a recombination value of $22{\cdot}3 \pm 4{\cdot}1\%$. Among the same *Dh* animals the *Dh–ln* recombination was $1{\cdot}9 \pm 1{\cdot}3\%$ and the *dr–ln* value was $24{\cdot}3 \pm 4{\cdot}2\%$.

PLEIOTROPIC EFFECTS

During the course of the linkage tests two previously undescribed pleiotropic effects of the *dr* gene became apparent.

The first of these effects to be noticed was a tendency to white spotting; many homozygous dreher animals have a partial belt of white. In families in which dreher was segregating but no known spotting genes were present, 54 out of 66 dreher young had some white spotting in the belt region whereas only 3 out of 103 non-dreher animals showed any. The effect in the drehers was confined to the belt region but was variable in extent. Of the 54 spotted drehers, 6 had a complete belt, 24 had ventral belts only, 16 had ventral belts which extended up the flanks, and 8 had merely belly spots. The three non-dreher animals with spotting had belly spots only; to find 3 out of 103 otherwise fully pigmented animals with belly spots is within the range of normal variation.

The second pleiotropic effect of the dreher gene to be noticed was a tendency to modify the expression of the gene brachyury (*T*). Animals of the genotype $T+\ drdr$ had on the average shorter tails than those of the genotype $T+\ +dr$ born in the same family. In the progeny of some matings segregating for *T* and *dr* the tail length of the brachyury animals was estimated by eye, as a fraction of the normal length. The non-dreher brachyurics in this stock typically had tails which were about nine-tenths of normal length, but the dreher brachyurics had in general tails of less than half normal. Table 4 shows that the mean of the estimated lengths of the non-dreher tails was 0·88 normal whereas that of the drehers was 0·38 normal.

Table 4. *Estimated lengths of tails of* T+ *animals heterozygous and homozygous for* dr, *expressed as tenths of normal length*

	No. of mice with tails of x tenths length											
Genotype	$x =$ 0	1	2	3	4	5	6	7	8	9	Total	Mean
$+dr$	—	—	—	—	—	1	1	3	7	47	59	0·88
drdr	11	5	7	9	8	8	3	2	5	6	64	0·38

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Such an interaction of *dr* and *T* was quite unexpected since *dr* alone had no externally visible effect on the tail or skeleton in general. Further, the interaction still remained unexplained when alizarin-stained preparations of the skeletons of three animals of each of the four types *T* + + *dr*, *T* + *drdr*, + + + *dr* and + + *drdr* were made. No skeletal abnormalities which could account for the effect were found.

In both these types of pleiotropism there were some drehers which did not show the effect. This could have two explanations. Either the pleiotropic effects in question show incomplete penetrance or they are not due to pleiotropy but to a gene linked to *dr*, the drehers not showing the character being crossovers. The second explanation is ruled out since the hypothetical complementary crossover types (non-dreher belted animals, or non-dreher *T* + animals with tails less than half normal length) were not found. Therefore the failure of some drehers to show the effects must be due to incomplete penetrance. It still remains possible that this was not a case of true pleiotropy but that genes very closely linked to *dr* were responsible. It seems best to accept the hypothesis of pleiotropy until it is disproved by the finding of true crossovers.

SUMMARY

Linkage studies with the mutant dreher (*dr*) of the mouse (*Mus musculus* L.) have shown that it lies in linkage group XIII and that the order of loci is *dr–Dh–ln*. The recombination between *dr* and *Dh* was 22·3 ± 4·1%.

Two previously undescribed pleiotropic effects of the *dr* gene were observed. The first was a tendency to white spotting in the belt region, and the second an interaction with brachyury (*T*) such that *drdr T* + animals had shorter tails on the average than + *dr T* +.

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