Theoretical and Applied Genetics 46, 135-142 (1975)
© by Springer-Verlag 1975
TAG 1314

Mottled Neuherberg (Mo^N), a New Male-lethal Coat Colour Mutation of the House Mouse *(Mus musculus)**

Johannes Horst Schröder

Institut für Biologie, Gesellschaft für Strahlen- und Umweltforschung, Neuherberg nr. München (BRD)

Summary. A new semidominant X-chromosomal mutation, *Mottled Neuherberg* (Mo^N), which causes coat colour variegation is described. Mo^N arose in the second postirradiation generation after 2 × 200 R of X-rays (24 hours apart) to oocytes of X/O mice. Heterozygous Mo^N females have irregular patches of fully and lightly coloured fur over the whole coat with curly vibrissae. Their viability is reduced, about 3% of the heterozygotes dying prenatally and 6 to 28% dying postnatally before weaning. Survivors are fertile without externally visible abnormalities. Hemizygous Mo^N males die *in utero* after implantation. The recombination frequency between Mo^N and *tabby* (Ta) was 3.65 ± 3.16% (with 95%-confidence limits). Therefore, it is suggested that Mo^N is a new allele of the *mottled* (Mo) locus of the house mouse. Mo^N-bearing ova seem to have a lower chance of becoming fertilized by wild-type spermatozoa than by Ta-bearing spermatozoa.

1. Introduction

X chromosome-linked mutations at the *mottled* locus of the house mouse *(Mus musculus)* seem to be very common (reviewed by Green, 1966). Four mutations of similar phenotype have been reported so far: *mottled*, Mo (Fraser et al., 1953); *brindled*, Mo^{br} (Falconer, 1956); *dappled*, Mo^{dp} (Phillips, 1961); and *viable-brindled*, Mo^{vbr} (Cattanach et al., 1969). In the cases of Mo and Mo^{dp}, all hemizygous males die *in utero* between the 11th and 17th day of gestation (Falconer, 1953; Phillips, 1961). Mo^{br} males usually die when two weeks old, but a few survive and are fertile (Fraser et al., 1953; Falconer, 1956). Mo^{vbr} males are viable but sterile and hence homozygous Mo^{vbr} females can not be produced (Cattanach et al., 1969). Heterozygous females exhibit a variegated or striped phenotype with irregular patches of fully and very lightly coloured fur over the whole coat due to X-chromosome inactivation (Lyon, 1961). Although allelism was impossible to prove by crossing tests because of male lethality or sterility, it was likely that most of these mutants arose by remutation at the same locus (Lyon, 1960; Welshons and Russell, 1959).

2. Materials and Methods

(i) First Occurrence of the Mo^N Mutant

The original *mottled Neuherberg* mutant (Mo^N) appeared as a single female in the second post-irradiation generation after 200 + 200 R of X-rays (24 hours apart, 50 - 60 R/min) to oocytes of adult X/O (+/O) mice. This second post-irradiation generation was obtained as follows. The irradiated +/O female was mated to an untreated *tabby* male (Ta/Y), and the resulting F_1 wild-type sons were then outcrossed with non-related Ta/O females. The first Mo^N female occurred within one litter together with non-Mo^N siblings (3 Ta/+ and 7 Ta/Y). Her F_1 father produced further normal outcross offspring (3 Ta/+, 3 +/O, and 4 Ta/Y) after mating with other Ta/O females.

(ii) Maintenance of Origin of the Mice

All the mice were bred and kept in Macrolon boxes and were 10-12 weeks old when mated. These boxes contained the animals which were collected for further breeding tests as well as the couples or dams with their young. The stable rooms were completely air-conditioned, at a temperature of 24 ± 2°C and atmospheric humidity of 55 - 60%. The artificial illumination was set automatically to a 12-hour rhythm. By this means, the seasonally-caused variation in average litter-size did not reach a significant level.

Inbred *tabby* males (Ta/Y) from the Edinburgh *tabby* stock and C3H or 101 inbred males were used as mates for the Mo^N females.

(iii) Mating Scheme

To determine the segregation ratio, litter-size reduction, and preweaning mortality, four types of crosses were performed. Heterozygous Mo^N females were either mated to wild-type C3H or 101 males (cross 1), or to *tabby* males (cross 2), and females heterozygous for both Mo^N and Ta (repulsion phase) were either mated to wild-type (cross 3) or to *tabby* males (cross 4). In crosses 3 and 4, male offspring were used to calculate the exchange frequency between Mo^N and Ta.

(iv) Identification of Phenotypes and Determination of Litter-Size and Preweaning Mortality

The identification of the different patterns of coat colour was not possible immediately after birth of the young mice, so was carried out after the beginning of hair growth. For the determination of litter size, however, all young were scored on the day of birth. All litters were weaned between the ages of 21 and 28 days. Dead young found during this period were taken into account for 'preweaning mortality'.

---

* Dedicated to Professor Dr. Otto Hug.

(v) Dissection of Pregnant Females

To detect embryonic mortality in pregnant Mo^N females, the uterine contents of heterozygous Mo^N females were compared with those of their wild-type sisters after mating them to non-related wild-type males. 13.5-17.5 days after the appearance of a vaginal plug, the females were dissected. The numbers of *corpora lutea* (CL), implants (IMP), resorbed embryos (RES), early deaths (ED), late deaths (LD), and living embryos (LE) were determined as described elsewhere (Schröder, 1969; Schröder and Hug, 1971).

(vi) Statistical Calculations

Analyses of variance were performed to compare the distribution of breeding and dissection data for the different crosses. Mean values were compared by the use of 95%-confidence limits according to the t-test (Weber, 1967). The significance of differences concerning sex-ratio, percentages in different phenotypical classes and preweaning mortality was calculated by the standard chi square method or by chi square in a 2×2 table. Yates' correction was applied for small sample sizes (Sachs, (1973).

3. Results

(i) Description of the Mo^N Mutant

The original Mo^N female mutant and all her Mo^N descendants resembled in both variegation of the coat colour and curling of the vibrissea the Mo mutant described by Fraser et al. (1953). The data on recombination frequencies of the new mutation and absence of mutant males favoured the assumption that it was a Mo-allele.

Heterozygous Mo^N females have irregular patches of fully and lightly coloured fur over the whole coat. There is great variation among Mo^N females, ranging from extended areas of whitish hair with relatively small patches of dark hair (Fig.1) to the reverse phenotype with more dark than light patches of fur. Females which are heterozygous for both Mo^N and the X-linked *tabby* gene (Mo^N+/+Ta) exhibit both types of variegation: the irregular patches of fully and lightly coloured fur characteristic for Mo^N are combined with the regular dark stripes which characterize heterozygosity for Ta (Falconer, 1953; Grüneberg, 1966) (Fig.2). Mice homozygous for Ta and heterozygous for Mo^N (Mo^N Ta/+ Ta) cannot be distinguished from homozygous *tabby* females (+Ta/+Ta).

(ii) Dissection Data

The comparison made of the uterine contents of Mo^N females and their wild-type sisters, both mated to non-related wild-type males, revealed a significant reduction of living embryos (27.97%) in Mo^N females. This was accompanied by a complementary increase in late (LD) and early deaths (ED) of embryos (Tables 1 and 2). No significant differences were found for the number of pregnant females or the number of corpora lutea (CL), implants (IMP), and resorbed embryos (RES) between Mo^N and wild-type females. The three fractions of dead embryos were summarized (RES + ED + LD) as "postimplantational losses" and computed against the " preimplantational losses" as the difference between CL and IMP (Table 3). The comparison shows that only the postimplantational losses were enhanced significantly in Mo^N females. This was due to the increase in ED and LD. Thus, it may be concluded from the dissection data that Mo^N male offspring were lost as early and late deaths.

(iii) Litter-Size Comparison

To determine litter size, segregation ratio and preweaning mortality, four different crosses were carried out

Fig. 1. Heterozygous Mo^N female mouse (Mo^N +/++) with the typical variegation of the fur colour and with curly vibrissae

Fig. 2. Double-heterozygous female mouse (Mo^N +/+ Ta) with variegated fur colour due to Mo^N and transverse striping which characterizes Ta heterozygotes

Table 1. Numerical values of the uterus contents of Mo^N and wild-type sisters after mating them to non-related wild-type males

Mating scheme		Corpora lutea (CL)	Implants (IMP)	Resorbed embryos (RES)	Early deaths (ED)	Late deaths (LD)	Living embryos (LE)
	No.	305	292	12	58 c)	9 d)	213 e)
$♀ \frac{Mo^N\ +}{+\ \ +} \times ♂ \frac{+\ +}{Y}$ a)	per pregnant female ± S. E.	9.53 ± 0.20	9.13 ± 0.17	0.38 ± 0.13	1.81 ± 0.31	0.28 ± 0.07	6.66 ± 0.38
	No.	256	246	6	7 c)	1 d)	231 e)
$♀ \frac{+\ +}{+\ +} \times ♂ \frac{+\ +}{Y}$ b)	per pregnant female ± S.E.	10.24 ± 0.31	9.84 ± 0.38	0.24 ± 0.11	0.68 ± 0.14	0.04 ± 0.04	9.24 ± 0.41

a) 33 mated and 32 pregnant females; b) 26 mated and 25 pregnant females; c)-e): significant differences

Table 2. Comparison of the distribution of uterus contents as found in Mo^N and wild-type sisters at dissection (cf. Table 1)

	♀ mates	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Comparison Mo^N *versus* $\underline{+}$
CL	Mo^N+/++	-	-	-	-	-	-	-	0	6	10	11	4	0	1	0	$F = 3.94$; $p > 0.05$
	++/++	-	-	-	-	-	-	-	1	3	1	11	5	2	1	1	
IMP	Mo^N+/++	-	-	-	-	0	0	0	0	9	13	7	3	0	0	-	$F = 3.50$; $p > 0.05$
	++/++	-	-	-	-	1	0	0	2	2	1	10	6	2	1	-	
RES	Mo^N+/++	24	5	2	1	-	-	-	-	-	-	-	-	-	-	-	$F = 0.59$; $p \gg 0.05$
	++/++	20	4	1	0	-	-	-	-	-	-	-	-	-	-	-	
ED	Mo^N+/++	10	6	4	7	4	0	0	1	-	-	-	-	-	-	-	$F = 20.96$; $p < 0.005$
	++/++	20	4	0	1	0	0	0	0	-	-	-	-	-	-	-	
LD	Mo^N+/++	23	9	-	-	-	-	-	-	-	-	-	-	-	-	-	$F = 6.05$; $0.01 < p < 0.05$
	++/++	24	1	-	-	-	-	-	-	-	-	-	-	-	-	-	
LE	Mo^N+/++	-	-	2	2	0	4	5	7	6	4	2	0	0	0	0	$F = 21.67$; $p < 0.005$
	++/++	-	-	0	0	1	0	1	3	3	3	9	2	2	1	-	

as described above. The highest average litter size was found in cross 2, the lowest in cross 4 (Table 4). The differences reached significant levels if one compared the distribution of litters of all 4 crosses to each other as well as those of crosses 1 *versus* 3, 1 *versus* 4, 2 *versus* 3, and 2 *versus* 4 (Table 5). Generally, heterozygous Mo^N females produce more young per litter when mated with *tabby* males than with wild-type males. On the other hand, dams heterozygous for both Mo^N and Ta have smaller litters than females heterozygous only for Mo^N (Table 4). This may be caused by reduced fertility of the double-heterozygous females and higher mortality of homo- and hemizygous *tabby* offspring of cross 4.

(iv) Segregation Ratio and Preweaning Mortality among Mo^N Offspring

Segregation ratio and preweaning mortality among the progeny of the four crosses with heterozygous Mo^N females are shown in Tables 6-9. The proportion of 'iden-

Table 3. Mean values of post- and pre-implantational losses ± S.E. for Mo^N and wild-type females (cf. Table 1 and 2)

Mating scheme	Postimplantational losses (RES + ED + LD)	Preimplantational losses (CL - IMP)
♀ $\frac{Mo^N +}{+ \; +}$ × ♂ $\frac{+ +}{Y}$	2.47 ± 0.43 a)	0.40 ± 0.26
♀ $\frac{+ +}{+ +}$ × ♂ $\frac{+ +}{Y}$	0.96 ± 0.18 a)	0.40 ± 0.49

a) Significant difference ($p < 0.05$)

Table 4. Distribution of litter sizes at identification for four different crosses with heterozygous Mo^N females (cf. Table 5)

Cross	Litters	Number of offspring per litter: 1	2	3	4	5	6	7	8	9	10	11	Mean ± S.E.
(1) ♀ $\frac{Mo^N +}{+ \; +}$ × ♂ $\frac{+ \; +}{Y}$	No.	0	8	8	15	24	26	21	8	3	2	0	5.51 ± 0.17
	%	0.00	6.96	6.96	13.04	20.87	22.61	18.26	6.96	2.61	1.74	0.00	
(2) ♀ $\frac{Mo^N +}{+ \; +}$ × ♂ $\frac{+ Ta}{Y}$	No.	1	2	4	8	13	10	12	12	2	2	1	6.02 ± 0.25
	%	1.49	2.99	5.97	11.94	19.40	14.93	17.91	17.91	2.99	2.99	1.49	
(3) ♀ $\frac{Mo^N +}{+ \; Ta}$ × ♂ $\frac{+ \; +}{Y}$	No.	9	6	8	5	10	10	6	5	4	1	0	4.73 ± 0.31
	%	14.06	9.38	12.50	7.83	15.63	15.63	9.38	7.81	6.25	1.56	0.00	
(4) ♀ $\frac{Mo^N +}{+ \; Ta}$ × ♂ $\frac{+ Ta}{Y}$	No.	5	3	9	9	5	9	1	1	0	1	1	4.30 ± 0.34
	%	11.36	6.82	20.46	20.46	11.36	20.46	2.27	2.27	0.00	2.27	2.27	

Table 5. Comparisons made of the distribution of litter sizes at identification between four different crosses with Mo^N females (cf. Table 4)

Analysis of variance	Comparisons made between crosses: 1 vs. 2 vs. 3 vs. 4	1 vs. 2	1 vs. 3	1 vs. 4	2 vs. 3	2 vs. 4	3 vs. 4
F	7.92 7.92	0.29	5.75	12.73	10.31	17.61	0.81
p	0.005	> 0.05	< 0.05 > 0.01	< 0.005	< 0.005	< 0.005	> 0.05

tified deaths' is included in the fraction of 'living mice at identification'; 'unidentified deaths' are not considered in the column of 'living mice at identification'.

According to the dissection data (Tables 1-3), the deficiency of Mo^N males was explained in terms of the action of a recessive X-linked lethal gene which was identical with the Mo^N mutation itself or at least closely linked to its locus. Under this assumption a sex ratio of 2 ♀♀ : 1 ♂ was expected, i.e., about 33.3% heterozygous Mo^N female offspring should occur in all crosses. This was found to be true for crosses 2-4 in which maternal and/or paternal Ta-carrying gametes were involved (Tables 7-9). Among the progeny of cross 1, however, significantly fewer Mo^N females than expected

Table 6. Segregation ratio and preweaning mortality among the offspring of cross 1 (♀ Mo^N +/+ + × ♂ + +/Y)

Parents		Offspring							
Cross 1:		Living mice at identification			Preweaning mortality				
♀ $\frac{Mo^N\ +}{+\quad +}$ × ♂ $\frac{+\ +}{Y}$					Identified phenotypes			Unidentified phenotypes	
		Mo^N+/++	++/++	++/Y	Mo^N+/++	++/++	++/Y	♀♀	♂♂
obtained	No.	138 a)	227a)	243a)	b) 39c)	b) 4	9c)	17d)	3d)
	%	22.70	37.34	39.97	28.26	1.76	3.70	4.45	1.22
expected	No.	202.67a)	202.67a)	202.67a)	11.80	19.42	20.78	-	-
obtained after correction	No.	159.6e)	227.0e)	246.0e)	-	-	-	-	-
expected after correction	No.	210.87e)	210.87e)	210.87e)	-	-	-	-	-

a) - e): Significant differences from the expected segregation ratio:
a): $\chi^2 = 31.9$; $p = 10^{-7}$; b): $\chi^2 = 41.8$; $p = 2 \cdot 10^{-10}$; c): $\chi^2 = 52.0$; $p = 10^{-10}$;
d): $\chi^2 = 41.3$; $p = 10^{-10}$; e): $\chi^2 = 19.6$; $p = 6 \cdot 10^{-5}$.

Table 7. Segregation ratio and preweaning mortality among the offspring of cross 2 (♀ Mo^N +/++ × ♂ + Ta/Y)

Parents		Offspring							
Cross 2:		Living mice at identification			Preweaning mortality				
♀ $\frac{Mo^N\ +}{+\quad +}$ × ♂ $\frac{+\ Ta}{Y}$					Identified phenotypes			Unidentified phenotypes	
		Mo^N +/+ Ta	+ Ta/+ +	+ +/Y	Mo^N +/+ Ta	+ Ta/+ +	+ +/Y	♀♀	♂♂
obtained	No.	126	130	140	19a) b)	0a)	2b)	1	0
	%	31.82	32.83	35.35	15.08	0.00	1.43	0.39	0.00

No significant difference with respect to the 1 : 1 : 1-segregation ratio.
a): $\chi^2 = 16.3$; $p = 6.10^{-5}$; b): $\chi^2 = 12.8$; $p = 0.0003$

Table 8. Segregation ratio and preweaning mortality among the offspring of cross 3 (♀ Mo^N +/+ Ta × ♂ ++/Y)

Parents		Offspring										
Cross 3:		Living mice at identification						Preweaning mortality				
♀ $\frac{Mo^N\ +}{+\ Ta}$ × ♂ $\frac{+\ +}{Y}$		Living non-exchange mice			Living exchange mice			Identified deaths			Unidentified deaths	
		Mo^N +/++	+ Ta/++	+ Ta/Y	Mo^N Ta/++	++/++	+ +/Y	Mo^N+/++	+Ta/++	+ Ta/Y	♀♀	♂♂
obtained	No.	78	94	87	2	7	4*	17a)	0a)	3	13	4
	%	28.68	34.56	31.99	0.74	2.57	1.47	6.57	0.00	3.30	6.16	4.21

No significant difference with respect to the 1:1:1 -segregation ratio
a): $\chi^2 = 16.4$; $p = 5 \cdot 10^{-5}$
* Recombination frequency in male offspring (Mo^N - Ta): 4/91 = (4.40 ± 4.20)% (95%-confidence limits)

Table 9. Segregation ratio and preweaning mortality among the offspring of cross 4(♀ Mo^N +/+ Ta × ♂ + Ta/Y)

Parents		Offspring										
Cross 4:		Living mice at identification						Preweaning mortality				
♀ $\frac{Mo^N+}{+\ Ta}$ × ♂ $\frac{+\ Ta}{Y}$		Living non-exchange mice			Living exchange mice			Identified deaths			Unidentified deaths	
		Mo^N+/+Ta	+Ta/+Ta	+Ta/Y	Mo^NTa/+Ta	++/+Ta	++/+Y	Mo^N+/+Ta	+Ta/+Ta	+Ta/Y	♀♀	♂♂
obtained	No.	46	47	45	0	13	1*	6	4	1	11	3
	%	30.26	30.92	29.61	0.00	8.55	0.66	13.04	8.51	2.22	10.38	6.52

No significant differences with respect to the 1:1:1-segregation ratio and to the preweaning mortality
* Recombination frequency in male offspring (Mo^N - Ta): 1/46 = (2.17 ± 4.20)% (95% -confidence limits)
Pooled data of cross 3 and 4: (Mo^N - Ta): 5/137 = (3.65 ± 3.16)% (95% -confidence limits)

were obtained (Table 6). Because no litter-size reduction was found in cross 1 compared with crosses 2-4 (Table 4), a selective preweaning mortality of Mo^N females could not be the main cause for the reduced percentage of Mo^N female offspring in cross 1. The reduction in Mo^N females was associated with a significant increase in preweaning mortality of unidentified females compared with unidentified males. Therefore, one can assume that a considerable number of Mo^N females died before the identification of the different phenotypes was possible. Moreover, less than 33.3% Mo^N females were obtained in all crosses, and the reduction of living embryos at dissection of Mo^N females exceeded the expected 25% loss due to prenatal death of Mo^N males. A combination of a slight prenatal lethality with postnatal death before identification may have led to the reduction of Mo^N females in cross 1. If so, the correction of the number of living Mo^N female offspring at identification of cross 1, by adding both the 17 unidentified dead females and the 2.97% surplus of prenatal deaths from the dissection data, as well as by the addition of the 3 unidentified dead males to the fraction of living males, would result in a corrected fraction of Mo^N females which should approximate to the expected number. However, despite this rather sophisticated procedure the corrected number of 159.6 Mo^N females (Table 6) did not fit the expected number of 210.9 Mo^N females.

The preweaning mortality of identified Mo^N female offspring of all 4 crosses showed higher values than that of their identified siblings. These differences reached a significant level in crosses 1-3 (Table 6-9). Because this higher preweaning mortality of identified Mo^N females was already included in the number of living Mo^N females at identification, this enhancement could not be responsible for the deficiency of living Mo^N females at identification in cross 1.

(v) Genetic Recombination between Mo^N and Ta

Since Mo^N +/++, Mo^N+/+ Ta, and Mo^NTa/+Ta females can not be distinguished phenotypically from each other with certainty, only the number of exchange-male offspring of crosses 3 and 4 was taken into account to calcule the genetic distance between Mo^N and Ta (Tables 8 and 9). It was calculated to be 4.40 ± 4.20 % (4/91) for cross 3 and 2.17 ± 4.20% (1/46) for cross 4, respectively. After pooling the data of crosses 3 and 4, a recombination frequency of 3.65 ± 3.16% (5/137) was obtained. These values, given with 95%-confidence limits, satisfy the known genetic distance of 4.0 cM between the loci Mo and Ta (Green, 1974).

4. Discussion

The only way to attack the problem of estimating the locus of a newly arisen X-linked mutation with male lethality is to determine the genetic distance between the mutant gene and already known X-chromosomal markers. In the present study, the recombination frequency between *mottled Neuherberg* (Mo^N) and *tabby* (Ta) favoured the view that the new mutational site occurred at the *mottled* (Mo) locus. From both the present breeding and dissection data as well as from the phenotypic variation of the heterozygous Mo^N females, it seems likely that the new mutation is an allele of Mo or even identical with the originally described mutation at this locus (Fraser et al., 1953). For instance, prenatal lethality of hemizygous

males characterizes the mutation at the *mottled* locus. As with Mo males, prenatal lethality of Mo^N males, as early and late deaths, was proven. Like heterozygous Mo females, Mo^N females are less viable than their non-Mo^N siblings, but all survivors are fertile. The vibrissae of heterozygotes are curly and the coat is not waved. All these features are common to Mo and Mo^N but are at variance with the other alleles described as mutations at the *mottled* locus (Mo^{br}, Mo^{dp}, and Mo^{vbr}). For Mo^{br} *(brindled)*, exceptional mutant males with gross abnormalities could be obtained which were then used to breed homozygous Mo^{br}/Mo^{br} females (Fraser et al., 1953; Falconer, 1956). Some of the heterozygous Mo^{dp} *(dappled)* females were found to have clubbing of the forefeet at birth, or, at weaning, a tendency to walk on the dorsal surfaces of the hind feet. Hemizygous Mo^{dp} males have been reported to die at about 17 days gestation, with banding and thickening of the ribs and distortion of the pectoral and pelvic girdles and limb bones (Phillips, 1961). The gene Mo^{vbr} (*viable-brindled*) produces a variegated or striped phenotype in the heterozygous female. However, hemizygous Mo^{vbr} males are usually viable but sterile (Cattanach et al., 1969) and hence Mo^N is clearly distinct.

The higher preweaning mortality of heterozygous Mo^N females could not be responsible for the reduced frequency of Mo^N female offspring among the progeny of Mo^N dams mated to wild-type or *tabby* males. Because this reduction was obtained in all crosses (Table 6-9), two possible mechanisms may be discussed. First, a preferential loss of chromosome sets bearing Mo^N- X chromosomes to the polar bodies during the meiotic divisions of the ova may occur in a similar manner as suggested for X/O mice (Cattanach, 1962). Consequently, fewer Mo^N than wild-type ova would be produced by the heterozygous Mo^N females. This mechanism could explain the lower frequency of Mo^N female offspring which was observed in all crosses, but it can not explain the differing yield of Mo^N offspring in the four crosses. Because the percentage of Mo^N females was lowest after mating heterozygous Mo^N dams to wild-type males (cross 1), and significantly increased whenever Ta-carrying gametes were involved (cross 2-4), selective fertilization of Mo^N, Ta and + bearing ova may be considered as a second mechanism. Thus, Mo^N ova could have a lower chance of becoming fertilized by + spermatozoa than do + ova (cross 1). In contrast, Ta spermatozoa may fertilize Mo^N and + ova almost equally (cross 2). However, Ta-bearing ova have a higher probability of being fertilized by + than by Ta spermatozoa. Selective fertilization might also be a possible reason for the difficulty in detecting radiation-induced recessive sex-linked lethal mutations in the germ cells of the mouse. Only Mo^{dp} appeared as a new mutation in a low-dosage gamma-irradiation experiment (Phillips, 1961). The present mutation to Mo^N also appeared in an irradiation experiment. It might have either arisen spontaneously or, less likely, been induced by X-rays. In the latter case, the phenotypic manifestation of the new mutation occurred one generation later than expected, which can not be explained in the present state of our knowledge. Mo^N was the only mutation with a lethal effect in males so far detected after screening more than 5,000 X-chromosomes for recessive sex-linked lethal mutations in our laboratory.

Acknowledgements

The author is gratefully indebted to Mdmes. E. Neubner, I.S. Otten, and K. Peters for conscientious technical assistance. Mdmes. A. Hrdina, M. Hrdina, and W. Kobza helped in carefully breeding the mice. The photographs of the mutant mice were taken by Mr. G. Goddeng. The author also wishes to thank Dr. I.D. Adler for helpful discussion.

Literature

Cattanach, B.M.: X/O mice. Genet. Res., Camb., 3, 487-490 (1962)

Cattanach, B.M., Pollard, C.E., Perez, J.N.: Controlling elements in the mouse X-chromosome. Genet. Res., Camb., 14, 223-235 (1969)

Falconer, D.S.: Total sex-linkage in the house mouse. Z. ind. Abst. u. Vererbl. 85, 210-219 (1953)

Falconer, D.S.: Mouse News Letter 15, 23 (1956)

Fraser, A.S., Sobey, S., Spicer, C.C.: *Mottled*, a sex-modified lethal in the house mouse. J. Genet. 51, 217-221 (1953)

Green, E.L. (Ed.): Biology of the Laboratory Mouse, New York-Toronto-Sydney-London: Mc Graw Hill Book-Company 1966

Green, M.C.: Linkage map of the mouse. Mouse News Letter 51, 7 (1974)

Grüneberg, H.: More about the *tabby* mouse and the Lyon hypothesis. J. Embryol. Exptl. Morph. 16, 569-590 (1966)

Lyon, M.F.: A further mutation of the *mottled* type in the house mouse. J. Hered. 51, 116-121 (1960)

Lyon, M.F.: Gene action in the X-chromosome of the mouse *(Mus musculus)*. Nature, Lond., 190, 372-373 (1961)

Phillips, R.J.S.: *"Dappled"*, a new allele at the *mottled* locus in the house mouse. Genet. Res., Camb., 2, 290-295 (1961)

Sachs, L.: Angewandte Statistik. Planung und Auswertung, Methoden und Modelle. Berlin-Heidelberg-New-York: Springer 1973

Schröder, J.H.: Dominant lethal mutations after irradiation of mouse spermatogonia with 600 R of X-rays. Int. J. Radiat. Biol. 16, 377-387 (1969)

Schröder, J.H.; Hug, O.: Dominante Letalmutation in der Nachkommenschaft bestrahlter männlicher Mäuse. I. Untersuchung der Dosiswirkungsbeziehung und des Unterschiedes zwischen Ganz- und Teilkörperbestrahlung bei meiotischen und postmeiotischen Keimzellenstadien. Mutation Res. 11, 215-245 (1971)

Weber, E.: Mathematische Grundlagen der Genetik. Jena: VEB Gustav Fischer 1967

Welshons, W.J., Russell, L.B.: The Y-chromosome as the bearer of male determining factors in the mouse. Proc. Natl. Acad. Sci. U.S.A. 45, 560-566 (1959)

Received October 22, 1974
Communicated by W. Seyffert

Univ.-Doz. Dr. J.H. Schröder
Institut für Biologie

Gesellschaft für Strahlen- und Umweltforschung
Ingolstädter Landstraße 1
D-8042 Neuherberg bei München (Germany/BRD)