

ABNORMAL INHERITANCE OF THE SEX-LINKED TABBY GENE

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Summary

Females of unexpected phenotype occur occasionally in mouse stocks segregating for sex-linked genes. Data from breeding of such females and frequency of occurrence in several different stocks are given. A possible explanation is advanced to account for the discrepancies between genetical and histological observations.

I. INTRODUCTION

In mouse stocks segregating for sex-linked genes, unexpected females of homozygous or hemizygous appearance occasionally occur. Russell, Russell, and Gower (1959) have shown that these cannot be the result of (a) change in dominance, (b) high mutation rate, or (c) sex reversal. Welshons and Russell (1959) demonstrate that it is improbable that the cause is an XXY -chromosome constitution, leaving the possibility that these females lack all or part of an X -chromosome. McLaren (1960) confirms these results although her frequency of occurrence of abnormal females is much lower. She suggests that the XXY constitution is male but only one animal of this apparent genotype was found. She also points out there is evidence in human beings, the only other mammals for which data on unbalanced sex-chromosome constitutions are available, that XO is a sterile female and XXY a male-type intersex.

White (1960) considers it probable that the Y -chromosome carries male determining factors in all mammals and that the few species previously reported to have XO males are really the result of chromosome fusion.

II. MATERIALS AND METHODS

In this Laboratory several selection lines segregating for tabby, a sex-linked, semi-dominant mutant, are being maintained. Heterozygous tabby mice typically have a striped coat and the number of secondary vibrissae on the face is reduced from 19 to about 15 (range 10–19). In the homozygous and hemizygous condition the hair types are markedly abnormal and the coat appears silky, the number of secondary vibrissae is reduced to 9 (range 5–13), and there are other characteristics such as bare patches behind the ears, lack of hair on the tail, and narrow eyes.

The stocks have different backgrounds and have been kept for varying periods up to 5 years so that large numbers of tabby mice have been recorded. The mating system was such that no homozygous tabby females were bred. Nevertheless, females which resembled hemizygous males did occur.

Although the primary purpose of the stocks was not related to the problem of abnormal chromosome numbers, any unusual appearance was recorded. All mice

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were scored for secondary vibrissa number and this could be used as a check on general appearance. Females which resembled $Ta\cdot$ males had vibrissa scores in the range expected for $Ta\cdot$ males or $TaTa$ females. The phenotype of $Ta+$ animals can be considerably altered by selection and in some lines $Ta+$ females which are phenotypically indistinguishable from $++$ females are common. Therefore, although $++\text{♀} \times Ta\cdot\text{♂}$ crosses have produced apparently wild-type females, these have only been included from lines where $Ta+$ females can be distinguished consistently. In considering the frequency of occurrence in different stocks, only TaO females, i.e. females resembling homozygous females, have been included (the symbol " O " represents the absence of an X-chromosome or the occurrence of an abnormal X-chromosome, contrasting with the " \cdot " symbol which represents the Y-chromosome).

TABLE 1
FREQUENCIES OF NORMAL AND ABERRANT TYPES OF MICE IN DIFFERENT GROUPS OF STOCKS

Stock	Mating	Progeny						
		$Ta+$	$++$	$Ta\cdot$	$+\cdot$	TaO	$+O$	$Ta+\cdot$
Group 1	$++ \times Ta\cdot$	588	—	—	534	7	—	1
	$Ta+ \times ++$	484	477	424	442	19	—	—
Group 2	$++ \times Ta\cdot$	200	—	—	229	2	—	—
	$Ta+ \times ++$	173	174	164	179	2	—	—
Group 3	$++ \times Ta\cdot$	1809	—	—	1861	2	2	—
	$Ta+ \times ++$	1455	1442	1523	1538	5	—	1
Group 4	$++ \times Ta\cdot$	645	—	—	642	—	—	—
	$Ta+ \times ++$	347	311	323	312	—	—	—

III. RESULTS AND DISCUSSION

Table 1 gives the frequencies of normal and aberrant types in different groups of stocks. There are 15 stocks altogether but these fall naturally in origin and frequency of TaO females into four different groups. Group 1 stocks are those in which the tabby gene was backcrossed into inbred strains A, CBA, C57, DBA, and 101. All showed a high frequency of TaO females. Group 2 are selection lines based on a cross between CBA and 101. Group 3 are selection lines based on CBA, 101, and two non-inbred stocks which contained the tabby gene. This group includes the only lines in which $+O$ individuals could be identified with certainty. Group 4 are selection lines based on a large randomly bred stock. The correlation between the degree of inbreeding in the stocks and the frequency of XO females is very marked and is quite sufficient to explain the differences found by Russell, Russell, and Gower (1959), whose *scurfy* stock was inbred to allow ovarian transplants, and by McLaren (1960), whose stocks appear similar to our type 3.

A few *TaO* females have been mated; the results are given in Table 2 and confirm the results of Welshons and Russell (1959). If the aberrant females had been *TaTa·* when mated to a $+·$ the classes of progeny produced would be: *Ta+*, *Ta·*, *Ta+·*, *Ta··*, or more rarely *TaTa+*, *TaTa·*, $+·$, $··$. The only one of these genotypes which could possibly appear as a wild-type female is the *Ta+·*. As the apparently wild-type females did not transmit the *Ta* gene (no tabby mice were found in 29 progeny of two females) this hypothesis is untenable.

These data also show that in our stocks the egg lacking the *Ta* locus has a much lower viability than that found by Welshons and Russell. It is clear that the proportion of "wild-type" females produced by different *TaO* mothers varies (Table 2). This is also indicated in the data of Welshons and Russell (1959) where larger

TABLE 2
PROGENY OF *TaO* FEMALE MICE AFTER MATING WITH NORMAL MALES

Mating	Progeny			
	<i>Ta+</i>	$+O$	<i>Ta·</i>	$+·$
<i>TaO</i> \times $+·$	15	—	10	—
<i>TaO</i> \times $+·$	6	—	8	—
<i>TaO</i> \times $+·$	3	5	3	—

numbers of *TaO* females were mated although not many progeny were produced from each mating. This could be easily explained if "*O*" represents not lack of a whole chromosome but a deficiency, in which case it is only to be expected that a long deficiency would be less viable in an egg than a shorter deficiency.

Ohno, Kaplan, and Kinoshita (1959) have found with inbred strains no evidence of production of sperm either lacking X- and Y-chromosomes or possessing both X- and Y-chromosomes. They believe the occurrence of XO females is due to loss of an X-chromosome in early division. The data of Welshons and Russell and the breeding data given here show that *O* eggs can be functional although the viability varies. If *O* sperm do not occur there should be more *TaO* females from $++ \times Ta·$ matings than from *Ta+* \times $+·$ matings. In the former the *Ta* chromosome comes from the male and a loss or deletion of either of the $+$ chromosomes of the female can survive in the egg to produce a *TaO* female. These can also be produced by an error in cleavage. Any *TaO* females from *Ta+* \times $+·$ matings must have the *Ta* chromosome from the female parent and, if *O* sperm do not occur, must all represent the loss of an X-chromosome in early cleavage.

The data show 26 *TaO* females from *Ta+* \times $+·$ matings and only 11 from $++ \times Ta·$ matings. Either *O* sperm do occur or errors in cleavage are much more frequent when the mother is *Ta+*. In view of the difference in viability of *O* eggs

from different mothers it seems more likely that the former is correct but that the *O* sperm had only part of a chromosome missing and were not detected by the histological methods of Ohno, Kaplan, and Kinoshita (1959).

The striped male found by McLaren (1960) died before reaching maturity but she suggests that it was $Ta+$. Two more males of this type have appeared in our experiments; both were strong and healthy but although each was mated to several females known to be fertile, no offspring were produced. It was therefore not possible to confirm that these animals were XXY .

If the TaO females have a deletion of the Ta locus rather than lack of a whole chromosome there must be an exceptionally high rate of spontaneous deficiencies; particularly as this phenomenon has also been observed with *bent tail* and *scurfy*. However, until this possibility can be eliminated the grounds for assuming that the XO chromosome constitution is female are uncertain.

IV. REFERENCES

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ADDENDUM

Cytological examination by D. L. Hayman (University of Adelaide) shows that one male, presumed XXY , has $2n = 41$ chromosomes, and one aberrant female has $2n = 39$. She consequently lacks a whole chromosome and not part as suggested.