THE EXPRESSION OF THE TABBY AND CRINKLED GENES IN DIFFERENT GENETIC BACKGROUNDS IN THE MOUSE

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TWO mutants in the mouse, Tabby and crinkled, produce identical phenotypes when homozygous. The *Ta/Ta* or *cr/cr* mouse has a long, narrow face, a very smooth looking coat with bare patches behind the ears, no hair on the tail and a markedly reduced number of secondary vibrissae (FALCONER, FRASER and KING 1952). The coat of the mouse normally consists of four types of hair: guard hairs, awls, auchenes and zigzags (DRY 1962). Closer examination of the hair of *Ta/Ta* or *cr/cr* mice reveals that the coat consists entirely of one type of hair which resembles an awl in length and shape but lacks the orderly arrangement of pigment granules found in normal awls (Figure 1). The mutants differ in that

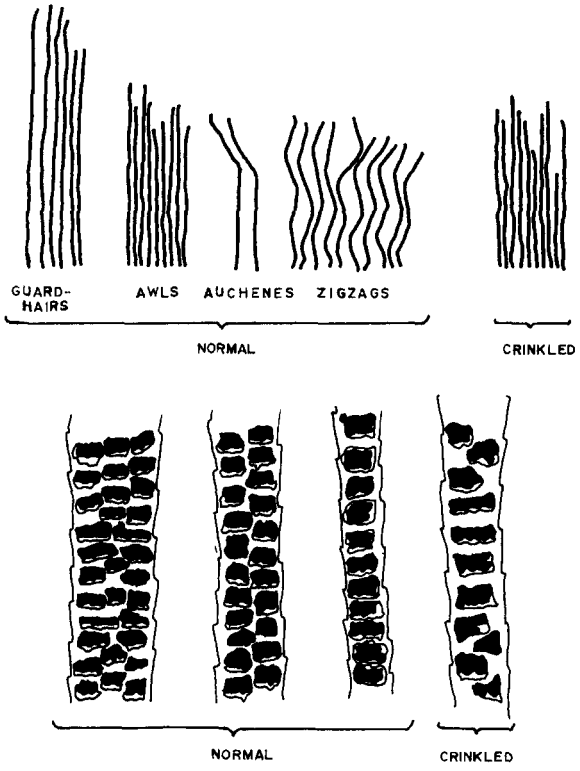

FIGURE 1.—Typical hair from normal and homozygous mice (after FALCONER, FRASER and KING 1951).

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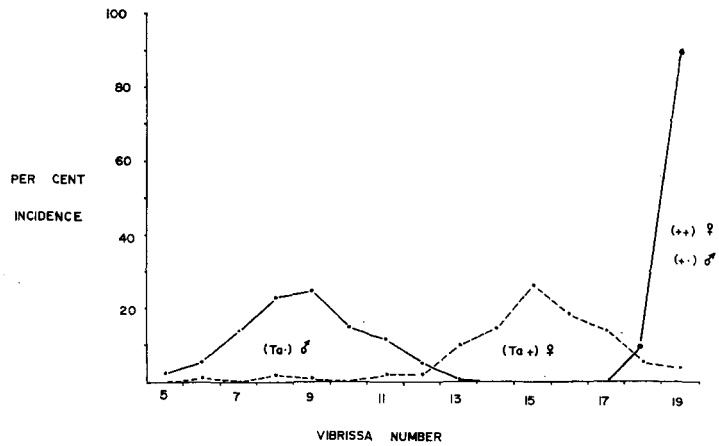

FIGURE 2.—Distribution of vibrissa numbers in unselected +/+ (or +/Y), *Ta*/+ and *Ta*/Y mice.

crinkled is an autosomal recessive and Tabby, a sex linked semi-dominant. *Ta*/Y males are phenotypically identical with *Ta*/*Ta* females as far as can be determined, while *Ta*/+ females have striped coats and an intermediate number of secondary vibrissae.

The number of secondary vibrissae in a normal mouse is an almost invariant 19, but in the mutants there is an increase in variance accompanying the decrease in number (Figure 2). These vibrissae are distributed in groups on the face and fore limbs. Selection for high and low vibrissa number in Tabby mice has produced a clear response, not only in Tabbies but also in their non-Tabby sibs thus showing that there was genotypic variation underlying the phenotypic invariance of vibrissa number (DUN and FRASER 1959). After 15 generations of upward selection the modal vibrissa score of *Ta*/+ females was 19, the normal number, and at the same time the striping of the coat was reduced to such an extent that sometimes adult *Ta*/+ mice could not be distinguished from +/+. Thus as the mean vibrissa score approached the normal canalisation zone, the effects of the Tabby gene on both vibrissae and coat became less. At the same time, in the low line the stripes of *Ta*/+ females were very obvious and the mice often had long narrow faces and, when young, bare patches behind the ears. In other words, the dominance of the gene was changed in both directions by the selection in opposite directions.

The extreme phenotypes for Tabby and crinkled are indistinguishable and no interaction was found by FRASER, NAY and KINDRED (1959) i.e., *Ta*/+ +/*cr* mice resembled *Ta*/+ and all genotypes which included *Ta*/Y, *Ta*/*Ta* or *cr*/*cr* appeared similar. These authors only looked at the vibrissae of an unselected stock; no detailed studies were made of the hair which might show more subtle effects. By crossing the crinkled gene into the selection lines it was possible to compare the effects of these genetic backgrounds on *Ta*/Y and *cr*/*cr* animals and also to examine the hair and vibrissae of combinations of *Ta* and *cr*. *Ta*/+ *cr*/*cr*

and *Ta*/Y *cr*/*cr* were not included in this comparison because the production and identification of these genotypes in any quantity is difficult and is complicated in the low line by the reduced viability and fertility of the extreme phenotype.

MATERIALS AND METHODS

The mouse stocks used were produced by repeatedly backcrossing the *cr* gene to the high and low vibrissa selection lines, high selection Tabby (HST) and low selection Tabby (LST) and were designated HST*cr* and LST*cr*. +/+ or +/Y segregants from the selection lines were used for these matings for the first five generations and then Tabby mice were used. The number of secondary vibrissae was scored at 5 days of age and checked at 10 days using a desk lamp and dark background. Vibrissae that were less than half the normal length were not counted. The groups scored were supra-orbital, post-orbital, post-oral, inter-ramal and ulna-carpal.

Hair samples were taken from the rump region when the mice were 3 weeks old. At this age the first coat is fully grown and the second wave of hair growth has not begun. The hair types were analysed in the manner described by FRASER (1951); at least 300 hairs from each animal were counted. About 500 hairs from each *Ta*/+ mouse were scored in an attempt to average out differences between the agouti and non-agouti stripes. As these stripes are very narrow in 3 week old mice of these stocks, errors should not be great. Hairs were counted as abnormal if there was obvious disorganisation of the pigment granules. All counts were made by the same observer to ensure that bias in classification should be consistent.

RESULTS

After five generations the mean scores of +/+ mice from the backcross lines were very close to those of +/+ or +/Y from a comparable generation of the main selection line, indicating that the background genotype of each pair of lines was similar. The data from *cr*/*cr* males and females were pooled as there was no apparent difference. The correspondence between these and the selection lines *Ta*/Y males was again close (Table 1). The difference of 0.9 in the low line was entirely due to a single group of vibrissae, the post-orals. The generation of inbreeding necessary to produce *cr*/*cr* mice from the backcross lines was carried out without selection and is probably responsible for most if not all of the difference found because the post-oral score of *Ta*/Y males increased by 0.4 vibrissae after one generation of relaxed selection.

In unselected Tabby mice the mean vibrissa score for *Ta*/+ was roughly intermediate between +/+ and *Ta*/Y (Table 2). Selection for high vibrissa score

TABLE 1

Mean vibrissa scores of selection and backcross lines

Selection line	Genotype (crinkled)	High			Low		
		+/+ or +/Y	*Ta*/+	*Ta*/Y	+/+ or +/Y	*Ta*/+	*Ta*/Y
(1)	+/+	19.1	18.8	12.2	17.4	9.1	5.8
(2)	+/+	19.1	18.1	12.2	17.3	9.8	5.8
(2)	+/*cr*	19.1	18.4	11.4	16.6	9.9	6.8
(2)	*cr*/*cr*	12.4	...	...	6.7	..	..

(1) Tabby selection lines, HST and LST. (2) Backcross lines, HST*cr* and LST*cr*.

TABLE 2

Mean vibrissa scores of unselected mice (taken from FRASER, NAY *and* KINDRED *1959)*

Crinkled genotype	+/+ or +/Y	*Ta*/+	*Ta*/Y
+/+	13	9.4	6.6
+/*cr*	13	10.9	6.1

increased the difference (DUN and FRASER 1959), i.e. high selection reduced the effect of a single Tabby substitution while low selection increased the effect. This was paralleled by changes in the coat. Most *Ta*/+ mice could easily be classified as HST or LST according to the degree of striping of the coat. In fact some HST *Ta*/+ showed no striping at all.

FRASER, NAY and KINDRED (1959) found no difference between the vibrissa scores of +/+ and +/*cr* mice in an unselected stock and in the present study no difference was found in HST*cr*. In LST*cr* however the mean of +/*cr* mice was significantly lower than the mean of +/+ (Table 1). This suggests a change in the effect of the *cr* gene in parallel with the increasing expression of the *Ta* gene in the low line. At the *Ta*/+ level the scores of *Ta*/+ +/*cr* are slightly higher than those of *Ta*/+ +/+ in HST*cr* but not in LST*cr*. A similar effect was found by FRASER, NAY and KINDRED (Table 2) but was interpreted as the result of crossing two different stocks. At the *Ta*/Y level +/*cr* mice had higher scores than +/+ in LST*cr*. It should be noted that in the results of FRASER, NAY and KINDRED the ulnacarpal group was not scored making the normal No. 6 vibrissae less.

Coat characteristics: The frequency of auchenes in the coat of the mouse showed a proportionately greater response to selection on vibrissae than did the vibrissae themselves (FRASER and KINDRED 1962). The difference between +/+ and +/*cr* in LST*cr* also showed more clearly in the coat. Because making fibre arrays and counting hairs is extremely tedious, only ten mice were used in each group, but the difference between the means of 4.3% auchenes for +/+ and 1.8% auchenes for +/*cr* was significant and most mice could be classified as +/+ or +/*cr* on the basis of the frequency of auchenes with only a small chance of error. Again no significant difference was found in HST*cr*.

Mean estimates for frequency of auchenes, zigzags and abnormal hairs in *Ta*/+ +/+ and *Ta*/+ +/*cr* females are given in Table 3. There are differences

TABLE 3

Numbers of auchenes, zigzags and abnormal hairs in the coat, expressed as a percentage of the total hairs counted

	High			Low		
Genotype	Auchenes	Zigzags	Abnormal hairs	Auchenes	Zigzags	Abnormal hairs
+/Y +/+	4.7	78.9	0	4.3	76.3	0
+/Y +/*cr*	4.1	77.6	0	1.8	75.2	0
Ta/+ +/+	3.1	50.4	15.0	0.8	35.5	15.0
Ta/+ +/+	2.3	49.4	12.7	1.5	34.2	15.6

in frequency of zigzags associated with the stripes of *Ta*/+ mice (FALCONER 1953) so 300 to 500 hairs were taken in groups of 50 to 100 to ensure that both dark and agouti regions would be included. The coats of *Ta*/+ mice contain up to 50% of grossly abnormal hairs but only normal hairs have been included. In auchene frequency as in vibrissa score, the difference between +/+ and +/*cr* is evident. When the comparison of +/+ and +/*cr* is made in the presence of *Ta*/+, results are difficult to interpret but this is very likely due to the numbers of abnormal hairs in *Ta*/+. The commonest of these resemble those of *Ta*/*Ta* and *cr*/*cr* but there are also zigzags with two rows of pigment granules and auchenes with a single row of granules on one side of the constriction. These demonstrate that the hairs not usually formed in homozygotes (FALCONER, FRASER and KING 1951) are also affected by the mutant genes.

In LST*cr*, where there was a range of vibrissa scores, the percentage of abnormal hairs was negatively correlated with the vibrissa score. The correlation coefficients for *Ta*/+ +/*cr* and *Ta*/+ +/+ were −0.39 and −0.32 respectively. Only the former was significant. Correlation coefficients could not be calculated for the high line since most animals have vibrissa scores of 19, but there were just as many abnormal hairs as in the low line and the same types occurred in about the same proportions. The few animals with lower vibrissa scores also tended to be the ones with the greatest number of abnormal hairs. In both high and low lines all three types of abnormal hair occurred through the whole range of vibrissa scores. It may appear contradictory that there should be a within line correlation when the numbers of abnormal hairs in the high and low lines were similar but it was only vibrissae that were under selection and it has been shown (FRASER and KINDRED 1962) that the canalisation of vibrissae and hair is different.

DISCUSSION

The reduction of vibrissa scores in low Tabby selection (LST) means that the scores of all mice were moved away from the normal canalisation zone at 19. Furthermore, the strength of canalisation is reduced in LST (KINDRED 1963). Under these conditions the *Ta*/+ phenotype became more extreme and the +/*cr* phenotype became distinguishable, i.e. crinkled was no longer completely recessive. Thus dominance, or the magnitude of the effect of the substitutiion of a mutant for a normal gene, depends not only on the action of the mutant but also on a developmental system which acts to reduce phenotypic variation. Dominance modification is well known and is claimed by FORD (1964) to be common in wild populations. As dominance causes more individuals to have the same phenotype, it is a means of reducing phenotypic variation. Canalisation also reduces phenotypic variation and it is interesting that selection for low vibrissa number has reduced both canalisation and dominance. If selection for dominance modification is as strong as FORD suggests, selection for canalisation may also be much stronger than has been supposed.

The action of crinkled in actually counteracting the effects of Tabby was most unexpected. It would have seemed more reasonable if mimic mutants had rein-

forced one another. However, if *Ta* and Ta^+ should be competing for a substrate neither may be getting enough to be effective in hair production and upsetting the balance in either direction could be an improvement.

In HST *Ta*/+ the reduction of striping is probably due to an increase in the number of zigzags in the coat. As zigzags always have a sub-terminal yellow band they contribute considerably to a normal looking agouti coat. However, although the coat appears more normal, there are just as many abnormal hairs in LST. Selection on vibrissa number has changed the number of vibrissae, the frequencies of hair types (particularly auchenes) in the coat, the striping of the coat and the dominance of the Tabby gene as it is reflected in these characters, but abnormality in the internal structure of the hairs has not been affected. It seems that there may be two aspects to the action of the Tabby mutant, only one of which has been influenced by selection.

SUMMARY

The autosomal gene crinkled (*cr*) was crossed into stocks which had been selected for high and low vibrissa number in Tabby (*Ta*), a sex linked mutant. The extreme phenotypes of Tabby and crinkled are identical. The vibrissa scores of *cr*/*cr* mice are very similar to those of *Ta*/Y from the same stock and there is also a similarity in the effect on the dominance of the mutant.

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