INHERITANCE OF HAIR CONSTRICTIONS IN MICE¹

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ABSTRACT

The frequencies of multi-constricted hairs in the pelage is the same (75%) in the caudal mid-dorsum of C57BL/10 and CBA inbred mice, but there are more single-constricted hairs in C57BL mice (9.41%) than in CBA mice (0.13%). This structural feature is used as a basis for genetic analysis of the hair coat.——The frequency of single-constricted hairs (4.41%) in F₁ mice is intermediate between the frequencies observed in the CBA and C57BL parent strains. Data from the F₂ crosses and backcrosses to the respective parent strains indicate that the presence of numerous single-constricted hairs in the pelage is an inherited characteristic. The mode of inheritance is controlled primarily by a semi-dominant autosomal gene (*single-constriction*; *Hct*), without the involvement of maternal factors.

ALTHOUGH numerous reports describe abnormal hairs in mice that have single-point mutations affecting hair growth (GREEN 1966), little is known about the inheritance of hair characteristics in the various inbred strains. Generally, hairs of the mouse are divided into two major categories (STRAILE, MANN and COLE 1972): long-tipped hairs, which consist of tylotrichs and bristles; and short-tipped hairs, which are subdivided into non-constricted (awl), single-constricted (auchene) and multi-constricted (zigzag) hairs. The frequencies of the various hair forms are variable, and several estimates have been reported (DRY 1926; CHASE and RAUCH 1950; FRASER 1951; SLEE 1957; FRASER and KINDRED 1962). Long-tipped hairs range from 1.6 to 2.5%, non-constricted short-tipped hairs from about 9 to 26%, single-constricted hairs from 0 to 7% and multi-constricted hairs from 70 to 83%.

Depending on the investigator, single-constricted hairs are recognized as a distinct type, are combined with the non-constricted short-tipped hairs (DRY 1926; FALCONER, FRASER and KING 1951; SLEE 1957) or are combined with the multi-constricted hairs (MANN 1962; SLEE 1965). The frequencies of single-constricted hairs differ markedly among inbred strains. For example in C57BL mice, single-constricted hairs comprise 6.5% of the pelage in the mid-dorsum after completion of the first growth cycle (STRAILE *et al.* 1972) and 7.8% of the new hairs that grow in the adult after removal of all resting club hairs (CHASE and RAUCH

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1950). STRAILE *et al.* (1972) found a few single-constricted hairs in C₃H and CBA mice after completion of the first growth cycle, but GALBRAITH (1964) did not observe single-constricted hairs in C₃H mice until after the third growth cycle. FRASER (1951) reported that single-constricted hairs ranged from 0.96% to 3.17% in four different strains, but many of the samples from individual mice contained no single-constricted hairs.

Several findings suggest that the frequency of single-constricted hairs is strain specific and therefore may be an inherited characteristic. After completion of the first growth cycle, the frequency of single-constricted hairs is consistently higher in C57BL than in CBA mice (STRAILE *et al.* 1972), whereas the number of hair follicles per surface area is the same in both strains. Comparisons between the two strains indicate that the same follicles that grow single-constricted hairs in C57BL mice grow non-constricted hairs in CBA mice.

The present study demonstrates that the frequency of single-constricted hairs is controlled genetically and probably is transmitted by a single autosomal gene.

MATERIALS AND METHODS

The CBA/Man (F135) inbred strain of mice was obtained from L. C. STRONG in 1961, and the C57BL/10 (F? +10) inbred strain was obtained from the Jackson Laboratory in 1964.

Samples of hair were removed from five male and five female CBA/Man and C57BL/10 inbred mice, from 31 offspring of the F₁ generation and from 36 offspring of the F₂ generation. Samples of hair also were removed from 35 progeny of the backcross generation to the C57BL parent strain and from 41 progeny of the backcross generation to the CBA parent strain. Hairs also were examined from mice of the C₃H, CHI, C, A, BRVR, I, and BALB/c inbred strains.

Since marked differences occur in the frequencies of different hair forms in various body regions, all of the hair samples were removed from a central-dorsal area of integument located 1 cm from the base of the tail in mice between 21 and 25 days after birth. At this time the hair follicles had completed the first growth cycle, and the hairs with anchoring clubs were embedded in resting follicles.

Hair samples were mounted on double-coated cellulose transparent tape attached to a white background. Hairs were aligned in rows and examined under low power magnification. During examination, individual hairs could be removed easily from the tape and could be remounted with aid of fine watch-makers forceps. All hairs in the sample were mounted to avoid biasing any one form. The number of hairs examined in each animal ranged from 499 to 1158 with an average of 761. In a total of 201 male and female mice, 150,707 hairs were examined.

The hairs were subdivided into multi-constricted, single-constricted and non-constricted categories. Long-tipped and short-tipped non-constricted hairs were included together in the latter category.

RESULTS

Hair characteristics that differ between the parent CBA and C57BL strains: The frequencies of multi-, single-, and non-constricted hairs are the same in male and female mice in both of the parent strains and in the various intercrossed and backcrossed animals. Thus the data in Figure 1 and Tables 1 and 2 are combined results of both sexes.

The frequencies of multi-constricted hairs are the same in C57BL and CBA mice, but the frequencies of single- and non-constricted hairs differ markedly between the two (Table 1). The coats of C57BL mice consist of about 9% single-

FIGURE 1.—Frequency distributions of single-constricted hairs collected after the first growth cycle. Number of animals for each strain or cross is represented within parenthesis. BC is the abbreviation for backcross and Q_2 for the median.

TABLE 1

Frequencies of hair forms in mice resulting from crosses of C57BL and CBA mice

Cross	Number of mice	Total hairs examined in the caudal dorsum	Hair form		
			Multi-constricted*	Single-constricted*	Non-constricted*
CBA	10	7081	74.60 $\pm$ 1.60	0.13 $\pm$ 0.13	25.27 $\pm$ 1.53
C57BL	10	7097	75.46 $\pm$ 0.98	9.41 $\pm$ 0.75	15.13 $\pm$ 1.10
F ₁ (CBA $\times$ C57BL)	18	12694	73.84 $\pm$ 1.33	4.29 $\pm$ 0.65	21.87 $\pm$ 1.32
F ₁ (C57BL $\times$ CBA)	13	10810	75.02 $\pm$ 0.95	4.58 $\pm$ 0.75	20.40 $\pm$ 0.91
F ₁ (Total)	31	23504	74.34 $\pm$ 0.85	4.41 $\pm$ 0.47	21.25 $\pm$ 0.86
F ₂ (Total)	36	28705	74.84 $\pm$ 1.15	3.53 $\pm$ 0.95	21.63 $\pm$ 1.08
BC (F ₁ $\times$ CBA)	30	22845	73.86 $\pm$ 0.85	2.29 $\pm$ 0.52	23.85 $\pm$ 1.05
BC (CBA $\times$ F ₁)	11	7792	74.53 $\pm$ 1.78	2.64 $\pm$ 1.25	22.84 $\pm$ 1.39
BC to CBA (Total)	41	30637	74.03 $\pm$ 0.75	2.39 $\pm$ 0.47	23.58 $\pm$ 0.84
BC (F ₁ $\times$ C57BL)	23	16224	74.92 $\pm$ 1.17	7.09 $\pm$ 0.81	17.99 $\pm$ 1.20
BC (C57BL $\times$ F ₁)	12	9554	76.40 $\pm$ 1.67	7.55 $\pm$ 1.07	16.05 $\pm$ 1.27
BC to C57BL (Total)	35	25778	75.42 $\pm$ 0.94	7.25 $\pm$ 0.62	17.33 $\pm$ 0.92

* In percent $\pm$ 95% C.I.

constricted hairs, but the coats of CBA mice consist of less than 1% single-constricted hairs. Although few single-constricted hairs are found in CBA mice, suppression of this hair form is not complete. No single-constricted hairs were found in samples from five CBA mice. Second hair samples were removed from two of the five mice. In the second samples, two single-constricted hairs were identified among 726 hairs in one animal, and one single-constricted hair was found among 683 hairs in the other animal. The difference in the frequencies of single-constricted, as well as non-constricted hairs, between the two inbred strains is significant at the 1% level.

Hair characteristics in the F₁ and F₂ populations: Samples of hair from mice of the F₁ generation have the same frequencies of multi-constricted hairs as in the parent strains (Table 1). However the frequencies of single-constricted and non-constricted hairs are approximately half-way between those of the parent strains (Table 1, Figure 1). There is no overlap in the frequencies of single-constricted hairs in offspring of the F₁ population with those of either parent inbred strain (Figure 1). The results indicate that the presence of a single-constriction in the hair shaft is controlled genetically.

No differences were observed in the frequencies of the three forms of hair between mice of the two F₁ reciprocal crosses (Table 1). Similar results were observed in progeny of the reciprocal backcrosses to the CBA parent strain (Table 1). These results indicate a lack of involvement of maternal factors in the formation of single-constricted hairs.

The frequency of multi-constricted hairs is the same in mice of the F₂ generation as in mice of the inbred strains or F₁ generation (Table 1). Unlike the inbred strains or F₁ generation, mice of the F₂ generation have a considerable spread in the frequencies of single- and non-constricted hairs (Figure 1). If a single-

constriction in the hair is considered to be controlled by one gene, one fourth of the F_2 samples should have a low frequency of single-constricted hairs as in the CBA samples, one half should be intermediate as in the F_1 samples and one fourth high as in the C57BL samples. Lastly, the frequency mean of the F_2 population should be similar to that obtained in the F_1 . The mean obtained for the F_2 population ($3.53 \pm 0.95\%$) did not differ significantly from that of the F_1 ($4.41 \pm 0.47\%$). If the frequencies below or above the F_1 population are considered to be similar to the respective frequencies for the CBA or C57BL parent genotypes, there are three classes of frequencies consisting of a ratio of 11 (low): 21 (intermediate): 4 (high). On the basis of a calculated 1:2:1 ratio, there should be an expected ratio of 9:18:9. Adding the class that includes less than five individuals to the next larger class, there is an observed 15:21 ratio ($\chi^2 = 1.00$, $P > 0.3$), which falls within the limits of an expected 1:1 ratio.

Hair characteristics in the backcrossed populations: There are no changes in the frequencies of multi-constricted hairs from progeny of F_1 mice backcrossed to either the C57BL or CBA parents (Table 1). The progeny have a frequency of single-constricted hairs that is about halfway between the frequencies of the F_1 population and respective inbred strain (Table 1). The frequencies of individual single-constricted hair samples overlap either with the respective parent strain or the F_1 population (Figure 1). However, the frequencies of single-constricted hairs in progeny of the C57BL backcrosses do not overlap with those of the CBA parent strain. Conversely, there is no overlap between progeny of the CBA backcrosses with those of the C57BL parent strain (Figure 1).

If the presence or absence of a single constriction in the hair is controlled by one gene, one half of the hair samples in each of the backcrossed populations should have single-constricted hair frequencies that overlap with the appropriate parent strain, and one half of the hair samples should overlap with the F_1 population. If the frequencies below or above the F_1 populations are considered similar to the respective parent genotypes, there is an observed ratio of 18:17 in the C57BL backcrossed samples and 16:25 in the CBA backcrossed samples, both of which fit an expected 1:1 ratio.

Hair characteristics in seven additional inbred strains: The frequencies of multi-constricted hairs within the same body area are not the same among the seven strains examined (Table 2). The mean values of multi-constricted hairs in mice of the BRVR and I strains are above the confidence levels of mice in the CBA and C57BL strains, whereas the C and BALB/c are below. Except for the BRVR and C57BL inbred strains, one or more samples from mice in each of the remaining strains lacked single-constricted hairs. In strains other than C57BL, the highest number of single-constricted hairs found in any one hair sample was 9 among 614 hairs (1.47%). The findings suggest that the occurrence of a high frequency of single-constricted hairs as in C57BL mice, is the result of a genetic mutation.

DISCUSSION

The difference in frequencies of single-constricted hairs between mice of

TABLE 2

Frequencies of hair forms in nine inbred strains of mice

Strain	Number of mice	Total hairs examined in the caudal dorsum	Hair form		
			Multi-constricted*	Single-constricted*	Non-constricted*
C	5	3090	69.70 $\pm$ 4.00	0.57 $\pm$ 0.66	29.73 $\pm$ 4.11
BALB/c	5	3502	70.48 $\pm$ 0.70	0.51 $\pm$ 0.69	29.01 $\pm$ 0.99
A	6	4635	72.72 $\pm$ 1.74	0.29 $\pm$ 0.42	26.99 $\pm$ 1.82
C3H	6	4209	73.89 $\pm$ 1.54	0.15 $\pm$ 0.20	25.95 $\pm$ 1.53
CBA	10	7081	74.60 $\pm$ 1.60	0.13 $\pm$ 0.13	25.27 $\pm$ 1.53
C57BL	10	7097	75.46 $\pm$ 0.98	9.41 $\pm$ 0.75	15.13 $\pm$ 1.10
CHI	5	3509	77.44 $\pm$ 3.12	0.13 $\pm$ 0.18	22.43 $\pm$ 3.06
BRVR	5	4438	78.79 $\pm$ 1.46	0.69 $\pm$ 0.68	20.53 $\pm$ 1.39
I	6	4522	82.54 $\pm$ 1.81	0.07 $\pm$ 0.12	17.39 $\pm$ 1.90

* In percent $\pm$ 95% C.I.

the CBA and C57BL strains is most easily explained on the basis of a single semi-dominant autosomal gene, which will be called *hair constriction* (provisionally symbolized as *Hct*). However, suppression of single-constricted hairs is not complete in non-mutant mice, which suggests a possible interplay of genetic modifiers and environmental factors.

Selection of the C57BL and CBA strains for the present study, as well as in a previous study (STRAILE *et al.* 1972), was fortuitous. The frequencies of multi-constricted hairs in these strains are the same and do not effect measurements of other hair forms. A moderate increase in the frequency of multi-constricted hairs as observed in the I strain or decrease as observed in the C strain would complicate and possibly prevent a genetic analysis of the hair coat. Factors influencing higher or lower frequencies of multi-constricted hairs among mouse strains are unknown, but probably other parameters within the same system are controlled genetically.

The foregoing discussion indicates that caution must be exercised when interpreting quantitative data involving categories of hairs, particularly when information is incomplete. For example, no information presently is available concerning the genetic control of hair forms in the later hair growth cycles of older mice. Basic hair forms within a strain must be analyzed carefully in various body locations and at various ages. Even the techniques used to classify hair forms may cause variations in results (GRÜNEBERG 1966).

There is a lack of systematic data on the mechanisms that control hair follicle development, hair structure and regional hair patterns in "normal" mice. Experimental data on the various forms of hairs will continue to be ambiguous until the basic structure and function of the associated hair follicles and nerve endings are better understood. For example, even the apparently simple determination of when follicles stop being initiated in the mouse fetus remains in question (DRY 1926; FALCONER *et al.* 1951; FRASER 1951; MANN 1962; SLEE 1962; CLAXTON 1966). Since there are conflicting interpretations of available data on the dis-

tribution of hairs in "normal" mice, more complicated patterns of hairs in mutant mice, such as tabby (*Ta*), should be used with caution in formulating basic developmental concepts (GRÜNEBERG 1966, 1967; LYON 1968).

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