6. Studies on the Karyotype Differentiation of the Norway Rat. V

Hypotrichotic Mutant Rats Appeared in the Inversion Stock (LEM))*

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A rat stock "LEM" has been derived from the rats with inversion chromosome no. 1 (Yosida 1980a). These rats are characterized by the presence of the large metacentric pair no. 1 each of which is subtelocentric in the normal karyotype of the other strains. In this stock, a hypotrichotic mutant appeared spontaneously in the course of inbreeding. In the rats four hypotrichotic genes, designated hairless (*hr*), naked (*n*), fuzzy (*fz*) and nude (*nu*), have been reported by Robert *et al.* (1940), Castle *et al.* (1955), Palm and Ferguson (1976) and Festing *et al.* (1978). Viewed from the morphological characters in these mutant rats, the hypotrichosis appeared in the present inversion stock seems to be a new mutant, though the linkage tests are not yet been made between the other hypotrichotic rats.

Some preliminary notes are given in the present paper on the characters of the present hypotrichotic mutant with their genetic and chromosome analyses, referring to the occurrence of chromosomal and genic mutations in this rat strain.

Material and method. The LEM-stock here concerned originated from the hybrids between the Lewis and Long Evans strain rats. In a female of the Lewis-strain rat (LEW-1c), a translocation occurred between pair nos. 1 and 12 (Yosida 1980b). This rat was mated to a normal Lewis male (LEW-1C). One female (LEW-3d) out of the offspring was a mosaic consisting of two cell types, such as translocation/normal pair no. 1 and translocation/inversion pair no. 1 (Yosida 1980c). This female was crossed to a Long Evans-strain rat (LE-376B). In the offspring thus obtained the rats carrying inversion/normal pair no. 1 appeared by segregation. Among hybrids between these rats the inversion homozygotes were obtained. The rats with the inversion pair no. 1 constituted the LEM-stock

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(Yosida 1980a). The hypotrichotic mutant rats to be described in the following appeared in this stock (Fig. 1).

Fig. 1. Pedigree of LEM-stock rats originated from the hybrids between Lewis (LEW) and Long Evans (LE) rats. In the first generation (LEW-1c) the 1/12 translocation occurred and in the second generation (LEW-3d) the inversion developed to make the mosaic chromosome constitution. In the 8th generation corresponded to the 3rd generation of the LEM-stock, the hypotrichotic (bared) mutants occurred. tr, translocation; i, inversion; +, normal chromosome. Small letters (a, b...) indicate the females and the large letters (A, B...) the males.

The chromosomes of the hypotrichotic rats were investigated with the primary cultures of the tail tissue (Yosida 1980d).

Results. 1) *Characters of the hypotrichotic rat spontaneously appeared.* Two female hypotrichotic rats appeared in the first litter (LEM-26) from a mating between a female and a male in the LEM-17 litter. Further, 3 females and 3 males of a similar appearance were yielded in the litters, LEM-29 and 39, from the same parents (Fig. 1). The hypotrichotic rats were easily identified soon after birth because of slightly smaller size than the normal ones. They did not show normal hair growth in the young stage, though some fuzzy hairs were often observed in young and adult stages showing somewhat an irregular periodic cycle from fuzzy hair to almost complete hairless. The hairs, however, sometimes were confined to on the face appearing as striped pattern in the adult rat (Fig. 2).

At birth the body weight of the hypotrichotic rat was slightly lower than normal rats in males or females (Table I). An increase

Fig. 2. A new hypotrichotic (bared) mutant occurred in the LEM-stock rats. A: Young rats (20 days old). Two front rats are mutants and the rare one is normal in the same litter. B: Two months old mutant rat.

Table I. Body weight of hypotrichotic (bared) rats at birth

Characters	No. of rats		Average body weight
Normal (+/+ or +/ba)	♀	5	7.8 ± 0.25
	♂	3	8.6 ± 0.15
Hypotrichosis (ba/ba)	♀	2	7.3 ± 0.03
	♂	2	7.7 ± 0.1

in body weight from birth to the 70th day obtained in a hypotrichotic and normal males is given as example in Table II. The hypotrichotic rats are similar in general appearance to the nude rat, but the thymus was present in both new born and adult rats. The thymus, however, was slightly smaller in size than the normal one, being remarkable by rather yellowish colouration. The male and female hypotrichotic rats were fertile, and the female parents were able to lactate to the new born, though its ability seemed to be slightly inferior.

2) *Genetics*. Twenty-four rats were obtained in 3 litters from the same parents (LEM-17), among which 8 rats were hypotrichosis leaving 16 rats which were normal. The segregation ratio was not significantly different from the expected value (10 mutants and 18 normals), which was calculated based on the assumption that the present hypotrichotic rats were due to a simple and recessive mutant

Table II. Body weight of a normal male and a hypotrichotic (bared) male

Characters	Days after birth						
	Birth	10	20	30	40	50	70
Normal	8.6	21.2	48.4	109.9	165	220	300
Hypotrichosis	7.7	16.9	38.2	89.1	148	204	270

Table III. Segregation of hypotrichotic (bared) mutants in 3 litters born from the normal parents which are speculated to have a recessive bared gene (ba/+)

Characters	No. of rats observed (♀ : ♂)	Expected value
Hypotrichosis	8 (5 : 3)	6.0
Normal	16 (11 : 5)	18.0
Total no.	24 (16 : 8)	24.0 $\chi^2=0.75$ 0.5<p<0.3

Fig. 3. Karyotype of a female hypotrichotic (bared) mutant rat. Pair no. 1 is characterized by submetacentric chromosomes occurred by inversion of the normal subtelocentric, which is specific in the LEM-stock. All other chromosome pairs are apparently normal.

gene (Table III). In the cross between the hypotrichotic female and male, five rats were obtained, all of which were hypotrichotic. Evidence presented strongly suggests that the present hypotrichotic character is inherited by a simple and recessive mutant gene. This gene is tentatively designated "bared", with the gene symbol, *ba*.

3) *Chromosomes*. The chromosome constitution of the bared rats studied so far was characterized by a typical inversion pair no. 1 (Fig. 3), the pattern being the same as that of LEM-stock rats. Except the inversion, all other chromosomes of the bared rats were normal. This means that the bared (*ba*) rats were produced by gene mutation in the LEM-stock.

Remarks. Genetical hypotrichotic mutants of the rat have already been described by Robert *et al.* (1940) as hairless (*hr*), by Castle *et al.* (1955) as naked (*n*), by Palm and Ferguson (1976) as fuzzy (*fz*) and by Festing *et al.* (1978) as nude (*rnu*). It was shown that the young animal of the hairless rat was covered by hairs, normal in appearance, and that the beginning of loss of hairs occurred between 15 and 20 days of age (Robert *et al.* 1940). The situation is not compatible with the present bared rat. The naked young, unlike the hairless, had a scanty hair coat in the young stage, and the coat was lost at about three weeks after birth. According to Castle *et al.* (1955), the appearance and its loss of the fuzzy hair is repeated in cycles. The condition is similar to the present case. The fuzzy mutant is of rather similar nature to the naked one. This mutant has initially the sparse hair coat, but the hair rapidly becomes devoid. The skin fold of the mutant animals is marked in the neck region, in resemblance to that of the rhino (Palm and Ferguson 1976), with the feature somewhat different from that of the bared rat. According to Castle *et al.* (1955), the hairless (*hr*) and naked (*n*) genes are in the linkage group-III, while the fuzzy (*fz*) is in the linkage group-I (Palm and Ferguson 1976). The external feature of the bared rat is rather similar to the nude rat. The homozygote of the nude is recognized soon after birth by the presence of the bent vibrissae. The nude rat is also characterized by having the abnormal thymus rudiment. However the bared rat carried thymus, normal in appearance.

The hypotrichotic mutant in the rat is rather few in occurrence; about 4 mutants have been reported at present. In the present study, no linkage test has been done on the bared (*ba*) gene. Interesting is the fact that the present bared mutant appeared in the inversion no. 1 stock (LEM). In the LEM-stock a translocation occurred primarily between pair nos. 1 and 12, and then the inversion occurred in the next generation of a translocation heterozygous rat forming a mosaic chromosome constitution. The translocation probably caused an un-

balanced condition of pair no. 1, and then it acted as a trigger for inducing the inversion. The bared mutant appeared successively in the offspring of the inversion homozygotes. Though no linkage study has been made, it seems to the author that the *ba* gene might be associated with the chromosome no. 1. The linkage test in relation to the inversion has remained as future subjects. Based on the above investigations, it is probable that the chromosomal and/or gene mutations are possible to occur as a sequential event.

Summary. Hypotrichotic (bared) rats appeared in the LEM-stock of the Norway rats carrying inversion pair no. 1. Externally the mutant rats were of similar appearance to the nude rat, but they had thymus normal in appearance. Karyotypically the mutant rats were similar in pattern to the LEM-stock rats. The cross experiments have revealed that the bared character seems to be due to a simple and recessive gene (*ba*).

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