85. Studies on the Karyotype Differentiation of the Norway Rat. III

Segregation of Offspring from the 1/12 Translocation Heterozygotes and Fertility of the Translocation Homozygotes^{*)}

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In the previous paper some chromosomal data on the translocation between nos. 1 and 12 chromosomes found in a female Lewis-strain rat are presented (Yosida 1980a, b). This rat was heteromorphous for pair nos. 1 and 12 as a result of translocation and deletion. The translocation pair no. 1 was longer than that of the normal partner, but the pair no. 12 was shorter than the normal one due to the deletion. By mating with the normal Lewis-strain rat, this female produced 17 offspring from 3 litters. Among them 9 rats had normal homologous pairs, while 8 were heteromorphous for pair nos. 1 and 12. From the crosses between these F_1 rats, many specimens with the translocation heterologous and homologous pairs were obtained.

The present paper deals with the segregation of the translocation chromosomes of the rats produced by mating between the translocation heterozygous and normal rats, and also between the heterozygotes, with special reference to the fertility of the translocation homozygote animals.

Material and methods. The origin of the Lewis-strain rat (*Rattus norvegicus*) used was previously described (Yosida 1980a). To maintain the mutant chromosome in the offspring, and further to establish a stronger mutant stock, the hybrids between the Long-Evans and Lewis-strain rats with the mutant chromosome were produced. Then the study on the segregation of translocation chromosomes was carried out in the hybrid offspring thus obtained. The rat without the translocation was selected from the hybrids described above, and they were used as a control for the examination of fertility.

The chromosomes were investigated in cells of primary culture from tail tissues following Yosida (1980c).

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Results. 1) *Segregation of the 1/12 translocation chromosome.* In mating between the female 1/12 translocation heterozygotes (t/+) and the normal male (+/+), 89 rats consisting of ♀ 46 and ♂ 43 were obtained (Table I). In the offspring, rats with the normal karyotype (+/+) (Fig. 1) and those with the translocation heterozygotes (t/+) (Fig. 2) was segregated into 53 and 36. In the reciprocal mating 59 offsprings (♀ 33 + ♂ 26) were obtained. Their segregation into the normal (+/+) and the heterozygotes (t/+) was taken place with nearly the same frequency. In total, 148 rats were obtained; among them 83 rats had the normal karyotype (+/+) leaving 65 rats which had the heteromorphous pairs. The number of rats with the normal karyotype was slightly larger than that of the translocation heterozygotes, though it is not significantly different from the expected value.

Table I. Segregation of the offspring with the 1/12 translocation chromosome in the Norway rats

Parents	Offspring (F ₁)			
	+/+	t/+	t/t	Total (♀ : ♂)
♀ × ♂				
t/+ × +/+	53	36	0	89 (46 : 43)
+/+ × t/+	30	29	0	59 (33 : 26)
Total	83 (74)	65 (74)	0	148 (79 : 69) $\chi^2=2.2$ 0.2 < p < 0.1
t/+ × t/+	18 (17)	43 (34)	7 (17)	68 (33 : 35) $\chi^2=16.21$ p > 0.001

+/+, t/+ and t/t mean the rats with the normal karyotype, 1/12 translocation heterologous pairs and 1/12 translocation homologous pairs, respectively.

In mating between female and male heterozygotes, 68 rats (♀ 33 : ♂ 35) were obtained. They segregated into the following three categories; normal karyotype (+/+), heterozygotes (t/+) and the translocation homozygotes (t/t) (Fig. 3). The rats with the homologous pair no. 1 for translocation were always characterized by having the homologous pair no. 12 which is remarkable due to deletion. As seen in Table I the number of translocation heterozygotes was larger than that expected, while the number of the translocation homozygotes was smaller. χ^2 test revealed a significant difference between the observed and expected values.

2) *Fertility of the translocation homozygotes.* In the above cross experiments a considerable number of female and male rats carry-

ing the 1/12 translocation homozygous pairs were obtained. In mating between translocation homozygotes, all 148 rats from 16 litters so far obtained had always the 1/12 translocation homologous pairs (t/t), without showing other karyotypes. The average litter size of the rats with translocation was very high showing 9.2 ± 3.2 , and the sex ratio consisted of females 4.9: males 4.3 (Table II).

In the control rats having the normal karyotype based on the translocation heterozygotes, the litter size was 7.4 ± 3.3 in average of

Figs. 1-2. 1: Normal karyotype of the Norway rat (LEO-stock established from the hybrid between Lewis and Long Evans strain rats). Pair nos. 1 and 12 are ordinary subtelocentrics ($2n=42$). 2: Karyotype of a male with the 1/12 translocation heterologous pairs appeared in the hybrid between the Lewis and Long Evans strain rats ($2n=42$). Pair nos. 1 and 12 are heteromorphous in respect to the translocation and normal chromosomes (t/+) and the deletion and normal ones (d/+), respectively.

Figs. 3-4. Karyotype with the 1/12 translocation homologous pairs in the LET-stock rat derived from the hybrids between the Lewis and Long Evans strain rats ($2n=42$). 3: Metaphase. Thick arrows indicate the pair no. 1 with translocation. Thin arrows show the pair no. 12 characterized by deletion. 4: Karyotype. All chromosomes are homomorphic, but the morphology of the pair nos. 1 and 12 are different from the normal ones due to reciprocal translocation. The pair no. 1 is longer than the normal one, but the pair no. 12 is shorter. Translocation and deletion are shown by (t) and (d).

Table II. Litter size and sex ratio in the rats with 1/12 translocation homologous pairs

No. of litters counted	Total no. of rats	Average litter size
16	148 (♀78 : ♂70)	9.2±3.2 (♀4.9 : ♂4.3)

11 litters, the number of females and males in them being nearly the same.

Remarks. The translocation of chromosomes has been reported in human-beings (cf. Makino 1975), mice (cf. Altman and Katz 1979) and the black rat (Yosida 1980c), but no such information has been obtained so far in the Norway rat in both natural and laboratory productions. However, the translocation has frequently been known in malignant tumor cells (Yosida 1975) as well as in irradiated rats (Savkovic and Pecevski 1971). The translocation between pair nos. 1 and 12 occurring in the Lewis-strain rat seems to be of spontaneous origin. It seems to be a rare and peculiar case in the Norway rats under the laboratory condition. Interesting is that the fertility of the rats with 1/12 translocation was not reduced, but rather increased than that of the animals with the normal karyotype. If the 1/12 translocation would occur in the natural population, and the rats with the homologous pair would be produced, they might be over the population of the rats with the normal karyotype on account of their selective advantage. The occurrence of such a chromosome anomaly seems to be taken as an important factor in karyotype evolution and species differentiation in the Norway rat, the feature having been well demonstrated in the natural population of the black rats (Yosida 1980c).

The hybrid rats between the Lewis- and Long-Evans strains which have been characterized by 1/12 translocation homozygous pairs are tentatively indicated as a chromosome mutant stock, LET, and those without the translocation as a normal stock, LEO.

Summary. Segregation of 1/12 chromosome translocation occurring in Lewis-strain rats was studied with the data from mating between translocation heterozygous and normal rats. The translocation chromosomes segregated as expected in their offspring. In the offspring between the translocation heterozygotes, the number of the translocation heterozygotes was significantly larger, in contrast to the smaller number of the translocation homozygotes. Fertility of the translocation homozygotes, however, was rather superior in comparison with that of the normal rats.

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