EFFECT OF THE MATERNAL GENOTYPE ON THE FREQUENCY OF TRISOMY AMONG AUTOSOMES IN EMBRYOGENESIS

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Cytogenetic analysis showed that of 339 mouse embryos aged 8-10 days, heterozygous for the T_6 translocation, 78 were heteroploids. Trisomy (2n = 41) was found in 66 embryos, monosomy (2n = 39) in four, and triploidy (3n = 60) in eight embryos. The overwhelming majority (58) of heteroploid embryos had trisomy with respect to the T_6 marker autosome. The frequency of this type of trisomy in the progeny of females of different genotypes was 28.6% in C3HA/T_6 mice, 19% in CBA/T_6, 10% in C57Bl/T_6, and 8.9% in T_1IÉM/T_6 mice. These results indicate that separation of the chromosomes during meiosis in females heterozygous for the T_6 translocation does not take place at random but depends on the special features of the genotype.

The study of factors influencing separation of the chromosomes in meiosis is of great interest both to the study of the mechanisms of normal gametogenesis and to the explanation of the causes of chromosomal diseases [5, 7].

During maturation of the female gametes in Drosophila separation of the chromosomes is known not to take place at random but to be under genetic control [8, 13, 15]. The existence of genetic factors influencing segregation of meiotic chromosomes has also been postulated in mammals [6, 9, 14], but experimental verification of this hypothesis is lacking.

Mice with the T_6 translocation, with two marker autosomes in the karyotype in the homozygous state and only one in the heterozygous state [3, 11], are convenient objects with which to test this hypothesis. It has been shown that aneuploid gametes are formed in mice heterozygous for the T_6 translocation [10, 12]. Such males are sterile or semisterile, while the females are fertile and transmit aneuploidy to the embryos [3, 4]. Characteristically trisomy on account of the T_6 marker autosome has no effect on embryogenesis, i.e., all such aneuploid embryos survive [3]. The frequency with which embryos with T_6 trisomy are found in early embryogenesis can thus be used as an indicator of the frequency with which mature ova with this type of aneuploidy are formed.

During crossing of males homozygous for the T_6 translocation with females of different lines, animals with different genotypes were obtained in the progeny, and these mice were used to determine how the female genotype influences the frequency of formation of zygous with trisomy for the T_6 autosome.

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TABLE 1. Characteristics of Karyotypes of Normal and Malformed Embryos from Mice (♀) of Different Genetic Lines Heterozygous for the T_6 Translocation (results analyzed on the 8th-9th day of pregnancy)

Type of cross ♂	Type of cross ♀	Embryos	Embryos: Normal: 2n-40: abs.	2n-40: %	2n-40: total	2n-40: marker chromosome: present	2n-40: marker chromosome: absent	2n-41: total	2n-41: marker chromosome: present	2n-41: marker chromosome: absent	Malformed: abs.	Malformed: %
C57B	C57B/CBA—T_6	88	67	76,2	58	31	27	9	9	—	21	23,8
C3HA	C3HA/CBA—T_6	94	70	74,4	47	17	30	23	23	—	24	25,6
CBA	CBA/CBA—T_6	79	58	74,7	47	15	32	11	11	—	21	25,3
C3HA	T_1IEM/CBA—T_6	78	65	83,4	58	21	37	7	5	2	13	16,6

Type of cross ♂	Type of cross ♀	Embryos	Malformed: 2n-39: marker chromosome: present	2n-39: marker chromosome: absent	2n-40: total	2n-40: marker chromosome: present	2n-40: marker chromosome: absent	2n-41: total	2n-41: marker chromosome: present	2n-41: marker chromosome: absent	3n-60: total	3n-60: marker chromosome: present	3n-60: marker chromosome: absent
C57B	C57B/CBA—T_6	—	—	—	13	6	7	3	—	3	5	2	3
C3HA	C3HA/CBA—T_6	1	—	1	17	8	9	5	4	1	1	—	1
CBA	CBA/CBA—T_6	—	—	—	16	3	13	4	4	—	1	—	1
C3HA	T_1IEM/CBA—T_6	3	2	1	5	3	2	4	2	2	1	—	1

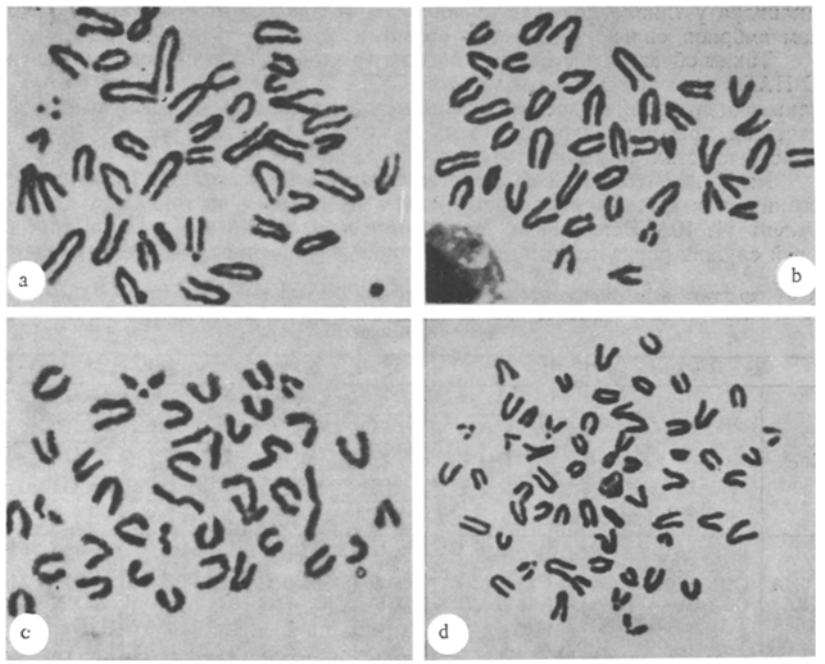

Fig. 1. Metaphase plates of embryos at the 8th-10th day of development from mice with T_6 translocation: a) trisomy for marker autosome T_6 (2n = 40; nf = 41), b) trisomy (2n = 41), T_6 marker autosome absent; c) monosomy (2n = 39); d) triploidy (3n = 60).

EXPERIMENTAL METHOD

Males of line CBA/T_6T_6 were crossed with females of lines C57B1, CBA, C3HA, and T_1IÉM*. Females were selected from the progeny, reared until sexual maturity, and then crossed with males of the normal parental line. The experiments were thus carried on females heterozygous for the T_6 translocation, and fertilized by males with a normal karyotype. The 1st day of pregnancy was taken to be the day when a vaginal plug was found. The females were sacrificed on the 8th-10th day of pregnancy and the number of corpora lutea in the ovaries and the number of implantation sites and of absorbed, living, and dead embryos in the uterus were counted. The embryos were taken from the membranes, examined under a binocular loupe, and chromosome preparations were then made [17]. Altogether 339 embryos were investigated. Fuller details of the methods of investigation were given previously [2-4].

EXPERIMENTAL RESULTS

The results are given in Table 1. Altogether 78 aneuploid embryos were found, 50 with a normal microanatomical structure. The number of heteroploid embryos in each group of mice differed significantly, and this was particularly marked as regards embryos with trisomy for the T_6 marker autosome. A pathological karyotype of this character was found altogether in 58 embryos, 48 of which had a normal microanatomical structure. This type of trisomy was found in the progeny of C3HA/T_6 females in 28.6% of cases, CBA/T_6 females in 19%, C57B1/T_6 in 10%, and T_1IÉM/T_6 in 8.9% of cases. The differences observed between groups with a high and low frequency of T_6 trisomy were significant for C3HA/T_6 mice ($P < 0.01$; $\chi^2 = 9.7$).

Another type of trisomy (without the T_6 marker chromosome) was observed infrequently: four of 261 embryos of C3HA/T_6, CBA/T_6, and C57B1/T_6 mice and four embryos of T_1IÉM/T_6 mice. Three embryos of the T_1IÉM/T_6 females were found to have monosomy. Monosomy was not found in the progeny of the C57BL/T_6 and CBA/T_6 mice, and only one embryo of 94 in the progeny of the C3HA/T_6 mice had monosomy. Phenotypically, all the embryos with monosomy consisted of small, round, trophoblastic vesicles in which the parts of the embryo could not be determined.

Eight of the 339 embryos studied had triploidy. The maximal number of triploids (five of 88) was found in C57B1/T_6 mice. The size of the germinal cylinder in the triploids as a rule was indistinguishable from the control, but the embryo itself was greatly retarded in its development.

The frequency of embryos with T_6 trisomy was thus highest in the C3HA/T_6 mice and considerably lower in the C57B1/T_6 and T_1IÉM/T_6 mice. The CBA/T_6 mice occupied an intermediate position between the groups with a high and low frequency of trisomy. The reason for these differences must probably be sought in the differences in behavior of the chromosomes in meiosis.

A quadrivalent is known to develop during meiosis in mice heterozygous for the T_6 translocation, and this may split up into a trivalent and a univalent [4, 10]. Naturally the frequency of formation of embryos with trisomy can act as an indicator of the frequency of appearance of the univalent, i.e., of mature gametes with an extra autosome. Probably among the various lines of mice on which these experiments were carried out the stability of the quadrivalent varies, i.e., the frequency of formation of the univalent in meiosis must be higher among C3HA/T_6 mice than among C57B1/T_6 mice. The possibility of specific elimination of aneuploid sets of chromosomes in the composition of the reduction bodies likewise cannot be ruled out [6], since this phenomenon, which takes place during the final stages of maturation divisions I and II, may also influence the frequency of formation of aneuploid embryos.

Further investigations are needed to determine which of these mechanisms is responsible for the differences found in the frequency of aneuploid embryos, which are evidence that the female genotype exerts a definite influence on the behavior of the chromosomes in meiosis.

*T_1IÉM is the name given to a colony of mice with spontaneous Robertson's translocation bred in the Department of Embryology, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR [1, 2].

LITERATURE CITED

1. V. S. Baranov and A. P. Dyban, Tsitologiya, No. 7, 820 (1971).
2. V. S. Baranov and A. P. Dyban, Ontogenez, No. 2, 164 (1971).
3. V. S. Baranov and A. P. Dyban, Ontogenez, No. 3, 248 (1970).
4. V. S. Baranov and A. P. Dyban, Genetika, No. 12, 70 (1968).
5. N. P. Bochkov and N. V. Glotov, Genetika, No. 3, 171 (1967).
6. K. N. Grinberg, in: Fundamentals of Human Cytogenetics [in Russian], Moscow (1969), p. 313.
7. A. A. Prokof'eva-Bel'govskaya, in: Fundamentals of Human Cytogenetics [in Russian], Moscow (1969), p. 11.
8. B. F. Chadov, Genetika, No. 2, 117 (1971).
9. B. M. Cattanach, Genet. Res., 3, 487 (1962).
10. C. E. Ford, in: Second International Conference on Congenital Malformations, New York (1964), p. 22.
11. C. E. Ford, J. C. Hamerton, D. W. H. Barnes, et al., Nature, 177, 452 (1956).
12. C. E. Ford and H. M. Clegg, Brit. Med. Bull., 25, 110 (1969).
13. R. F. Grell, Genetics, 44, 421 (1959).
14. R. C. Juberg and L. M. Davis, Cytogenetics, 9, 284 (1970).
15. L. Sandler, D. L. Lindsley, B. Nicolette, et al., Genetics, 60, 525 (1968).
16. J. Schroder, O. Halkka, and M. Brumner-Korventcontio, Hereditas (Lund), 65, 297 (1970).
17. J. Wroblewska and A. P. Dyban, Stain Technol., 44, 147 (1969).