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A mouse stock with 38 chromosomes derived from the reciprocal translocation T(7;15)33Ad

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Abstract

A reciprocal translocation T(7;15)33Ad with presumed breakpoints in bands 7A1 and 15F3 was induced in late spermatids by acrylamide treatment (5 x 50 mg/kg) of male (102/El x C3H/El)F_1 mice. The outcrosses of the original semisterile T(7;15) female generated 3 males monosomic for the short marker 7^{15} among a total of 15 males analysed. The Ms(7^{15}) males sired small litters and had reduced testes weights. From *inter se* matings of Ms(7^{15}) animals, nullisomic progeny for chromosome 7^{15} were obtained and mated. A breeding stock of mice with 38 chromosomes, homozygous for the long marker 15^7 and lacking the short 7^{15} marker, was established. Males and females with 38 chromosomes had the same body weight at weaning as the chromosomally normal mice of the same age; the adults had litters of normal size. For comparison the reciprocal translocation T(4;8) with similarly located breaks was analysed. No aneuploid progeny were obtained from the original semisterile T(4;8) female, balanced heterozygote males were sterile.

Fluorescent in situ hybridisation with major and minor satellite DNA probes and a telomere DNA probe produced all appropriate signals in the long and the short markers of both translocations. At the fusion sites the long markers 15^7 and 4^8 showed a bright signal with the major satellite DNA probe and no signal with the minor DNA probe, suggesting that the breaks occured within the pericentric heterochromatic block of chromosomes 7 and 8, respectively, presumably immediately below the centromere. Thus the long

markers constitute tandem fusions of the long arms of chromosomes 7 and 8 to the distal telomeric ends of chromosomes 15 and 4, respectively. The short markers 7^{15} and 8^{4} showed one signals with the major satellite DNA probe and 4 signals each with the telomere DNA probe. These observations indicate that the short marker 7^{15} which was lost had been a intact chromosome. The loss of the small chromosome 7^{15} was compatible with survival suggesting that no essential genes were located on the small reciprocal translocation product.

This is the first report of a fertile mouse stock with 38 chromosomes homozygous for a tandem fusion derived from a reciprocal translocation. The development of this tandem fusion stock is described as a laboratory example of one possible step in karyotype evolution.

Tandem chromosome fusions have played a significant role in karyotype evolution. Well studied examples are the Indian muntiac and the cotton rat (Imai, 1988; Elder and Hsu, 1988). The karyotype of the Indian muntiac (2n=6,7) evolved from a karyotype similar to that of the Chinese muntiac (2n=46) through a series of at least 17 tandem and three centromeric fusions (Liming et al., 1980; Elder and Hsu, 1988).

A characteristic type of tandem fusion in the mouse with only acrocentric-telocentric chromosomes is produced by reciprocal translocations with breaks near the centromere of one and the distal telomere of the other involved chromosome, i.e. c/t type translocations. In most cases the consequence is male sterility (Cacheiro et al., 1974). Heterozygous female carriers can give rise to aneuploid gametes by missegregation of the small marker chromosome during meiosis (Eicher, 1973). Two female mice with c/t type translocations (Adler 1990 and Adler, unpublished) observed in heritable translocation tests with acrylamide were bred and studied in detail.

For better determination of the break point location and to prove that the small translocation products were actually intact chromosomes the fluorescent in situ hybridization (FISH) technique was applied using satellite and telomere DNA probes. All pericentric heterochromatic blocks except the Y chromosome are labelled with the murine major gamma satellite DNA probe (Pietras et al., 1983; Weier et al., 1991, Miller et al., 1991). The murine minor satellite DNA Probe pmKC104 which contains a tandem repeat of 273 bp labels all chromosomes at the centromere near the kinetochore region (Wong and Rattner, 1988; Wong et al., 1990). In the mouse an exclusively telomeric labelling pattern has been reported for the telomere probe (Meyne et al., 1990; Schubert et al., 1992).

This paper describes the development of a fertile mouse stock with 38 chromosomes, derived from the reciprocal translocation T(7;15)33Ad after loss of the small marker chromosome. The reciprocal translocation T(4;8) is described for comparison. The break points of both translocations are characterized by FISH probes homologous to pericentric heterochromatin, the centromeric region and the telomeres.

Material and Methods

Origin of the reciprocal translocations T(7;15)and T(4;8)

The reciprocal translocation T(7;15) was induced in late spermatids by acrylamide treatment (i.p.) with five times 50 mg/kg, 24 h apart, of male (102/El x C3H/El)F_1 mice (Adler, 1990). The reciprocal translocation T(4;8) *(unpublished)* was induced in late spermatids by single acrylamide treatment with 100 mg/kg (i.p.) of male (102/El x C3H/El)F_1 mice (Adler, unpublished). The original heterozygote translocation carriers were females.

Breeding of the original translocation carriers

The original translocation females were mated to (102/El x C3H/El)F_1 males. Litters were counted and sexed at birth and male and female young were weaned at the age of 3 weeks.

Establishing the T(7;15) translocation stock

The breeding scheme is demonstrated in the pedigree (Figure 1). Among the male progeny of the original T(7;15) female only the monosomic [Ms (7^{15})] males were mated to (102/El x C3H/El)F_1 females. Their male and female Ms (7^{15}) progeny were selected for further breeding. The Ms (7^{15}) males were identified by cytogenetic analysis of diakinesis-metaphase I chromosomes of testis preparations. The Ms (7^{15}) females were identified by karyotyping the chromosomes from blood cultures. The Ms (7^{15}) animals were crossed *inter se* to determine if viable homozygous nullisomic progeny could be obtained. All 20 offspring of the *inter se* matings were karyotyped. The homozygous nullisomic mice were crossed *inter se* to maintain the line or outcrossed to (102/El x C3H/El)F_1 animals to determine the fertility. Each litter of the nullisomic mice and litters of the same size and age from normal hybrids were weighed at the age of 3, 4, 5, and 6 weeks.

Breeding of the T(4;8) translocation

Translocation carrying male and female offspring of the original T(4;8) female were identified by matings to (102/El x C3H/El)F_1 animals of the opposite sex followed by chromosome analysis. The heterozygous T(4;8) males were sterile. The reciprocal translocation line was maintained by mating semisterile T(4;8) females to (102/El x C3H/El)F_1 males.

Chromosome analysis

Male translocation suspects were weighed and orchidectomized unilaterally under ether narcosis. Testes were weighed before processing. For analysis of meiotic translocation multivalents testicular preparations of chromosomes at diakinesis-metaphase I were obtained according to the method of Evans et al. (1964). Bone marrow cells were prepared by the standard procedure (Adler, 1984) and short-term cultures of mouse peripheral lymphocytes were established by the techniques of Davisson and Akeson (1987). For karyotyping, mitotic chromosomes of bone marrow cells or peripheral lymphocytes were banded by the trypsin-Giemsa procedure (Gallimore and Richardson 1973). Presumed break points were determined using the standard mouse karyotype (Evans, 1989).

DNA probes

Heptameres of animal telomeric repeats (5'TAACCC-3') were synthesized in both sense and antisense orientation (Moyzis et al., 1988; Schubert et al., 1992), amplified and biotinylated in a polymerase chain reaction (PCR) (Ijdo et al., 1991).

The murine gamma satellite DNA probe (Saiki et al. 1988; Vissel and Choo, 1989), a gift from H. Zitzelsberger, GSF-Institut für Strahlenbiologie, Germany, was generated by primer directed in vitro amplification without plasmid purification as described elsewhere (Weier and Rosette, 1988; 1990). Biotinylation/ amplification of the murine gamma satellite probe was performed through mouse gamma satellite specific primers WSG1 (5'-CCCAAGCTTGAAATGTCCACT-3') and WGS2 (5'-CCCAAGCTTTTTCTTGCCATA-3') during 25 cycles with primer annealing at 50°C (Weier et al., 1991). The biotinylated probe DNA was stored without further purification at -20°C until used for in situ hybridization experiments.

The murine minor satellite DNA probe pMKC104, which represents a tandem repeat of 273 bp, in plasmid pTZ19U, was a gift from B. Vig, Reno, USA. It was amplified in *E. coli* JM103 and separated by CsCl gradient centrifugation (Wong and Rattner, 1988). The plasmid DNA was biotinylated by nick translation. One μg plasmid DNA in multiprimer buffer (25μl) containing 0.5μl of 40mM dATP, dCTP and dGTP, 1μl of biotin-dUTP (Sigma, B-7645), 2μl DNase (0,1 U/μl, Stratgene) and 1.5 μl of DNA polymerase I 5U/μl (Boehringer Mannheim) were incubated for 90 min at 16°C. Unincorporated nucleotides were subsequently removed with a Bio-Spin 30 column (Bio-Rad).

<u>Fluorescent in situ hybridization (FISH) and signal detection</u>

G-banded slides of the original T(7;15) female were more than 12 months old when used for in situ hybridization. They were pretreated in a pepsin/HCl solution (100μl/ml 0.01 HCl) at room temperature for 3-5 min. Freshly prepared slides of the T(4;8) and Ms(7^{15}) animals were stored up to 3 weeks at -20°C for before use. All slides were fixed in 4% paraformaldehyde in PBS plus 50 mM $MgCl_2$ for 10 min immediately before hybridization. Slides and probes were denatured for 10 min at 72°C in 70% formamide/2 x SSC (pH 7.0). Hybridization was performed at 37°C in humidified atmosphere overnight under coverslips sealed with rubber cement (Pinkel et al., 1986). The hybridization mix contained 50% formamide in 2 x SSC and 10% dextran sulphate. Approximately 20 ng probe per slide was added to the mix. E. coli tRNA (500μg/ml) was used as the carrier for the telomere probe. Herring sperm DNA (500μg/ml) was used as the carrier for the murine gamma satellite and minor satellite DNA probes. The slides were washed in 50% formamide/2 x SSC for the murine gamma satellite and minor satellite DNA probe, or in 30% formamide/2 x SSC for the telomere probe at 40°C for 40 min followed by two washes for 15 min each in PN buffer (0.1 M Na_2HPO_4, 0.1 M NaH_2PO_4, pH 8.0, plus Non-idet P40, final concentration 0.1%) at

37°C. Hybridization signals were detected with FITC-conjugated avidin for the murine gamma satellite DNA probe. The telomere and the murine minor satellite signals were detected with FITC-conjugated streptavidin with one round of amplification using biotinylated goat antistreptavidin antibody (Vector Laboratories). The slides were counterstained with propidium iodide (PI; 0.5 or 1 μg/ml, Sigma) in antifade solution (Johnson and Araujo, 1981). For detection of hybridization signals a Zeiss Axiophot fluorescence microscope was used with band pass filter 450-490 nm for simultaneous observation of FITC and propidium iodide fluorescence and band pass filter 510-560 nm for observation of propidium iodide. Photographs were taken on Kodak Ektachrome P800/1600 film and developed at 400, 800, 1600 or 3200 ASA depending on the intensity of the signals.

Results

Karyotype of the original translocation carriers

The karyotypes of G-banded metaphase chromosomes of the original translocation females were obtained from bone marrow preparations. In the case of T(7;15) presumed break points were located in 7A1 and 15F3. In the case of T(4;8) the presumed break ponts were located in 4D3 and 8A1. The resulting markers were the short chromosomes 7^{15} and 8^{4} and the long chromosomes 15^{7} and 4^{8} (Figure 2).

Breeding performance of the original translocation females

The females showed reduced fertility with average litter sizes of 4.9±0.6 young for T(7;15) and 3.0±0.5 young per litter for T(4;8) compared to similar control matings with an average litter size of 8.6. Among the 15 sons of the heterozygous T(7;15) female, 9 were tertiary trisomic [Ts(715)] and three were monosomic [Ms(7^{15})], two sons were normal and one was a balanced heterozygous translocation carrier (Figure 1). Thus, 80% of the male progeny were derived from aneuploid oocytes due to missegregation of the small chromosome 7^{15}.

Among the 9 sons of the heterozygous T(4;8) female there were five reciprocal translocation carriers and four chromosomally normal males. All reciprocal translocation males were sterile and had abnormal sperm. No monosomic and trisomic males were found in the original or any later matings of T(4;8) females.

Meiotic configuration of heterozygote male offspring

The testes weights of the males were corrected by dividing with body weight to compensate for the varying age at the time of preparation (6-12 weeks). The mean testis weight/body weight ratios was 3.0±0.4 for Ms (7^{15}) males, 2.9±0.4 for Ts(7^{15}) males and 3.2 for the T(7;15) male. The testis weight/body weight ratio of all three types of males were significantly reduced compared to the mean testis weight/body weight ratio of 3.7±0.4 for chromosomally normal litter mates (Table 1). The T(4;8) males had a significantly reduced testis weight/body weight ratio of 1.6±0.3 compared to an average of 3.3±0.6 for their normal litter mates (Table 1).

At diakinesis-metaphase I the T(7;15) males and the Ms (7^{15}) males showed 100% chain trivalents with or without the short univalent (Table 2). The Ts(7^{15}) males had 18% cells with 20 bivalents lacking the small univalent. Obviously, the tiny univalent was sometimes lost due to the preparation procedure. The metaphase I cells of T(4;8) males showed 55% chain quadrivalents and 43% chain trivalents plus a small univalent (Table 2).

Progeny of the Ms(7^{15}) animals

When outcrossed to (102/El x C3H/El)F_1 females the Ms (7^{15}) males were not sterile but sired small litters with an average of 4.5±0.4 young per litter (Table 3). When Ms (7^{15}) progeny were crossed *inter se* the average litter size was 3.0±0.2 young per litter. In these matings four mice, one male and three females, were found to be homozygous for the long chromosome 15^7 and nullisomic for the short marker 7^{15}, 10 mice were heterozygous for the long marker and lacking the short marker 7^{15}, 6 mice had a normal karyotype (Figure 1).

Homozygous nullisomic mice from T(7;15)

The mice homozygous for the long 15^7 marker and nullisomic for the short marker 7^{15} were crossed *inter se* or outcrossed. The litter sizes were near normal with an average of 7.0±0.8 young per litter for *inter se* crosses and 8.5±0.5 for outcrosses (Table 3). At weaning the body weight of 8.9±1.1 g (n=38) of the nullisomic offspring was not significantly different from the body weight of 9.0±1.1 g (n=72) of chromosomally normal mice of the same age. No differences between the body weight of nullisomic and normal mice were found when weighing ceased 3 weeks after weaning. The nullisomic mice were physically normal.

Fluorescent in situ hybridization (FISH)

With the murine major gamma satellite DNA probe the long marker chromosomes $15^7$and 4^8 showed two signals, one at the centromere of chromosome 15 or 4, respectively, and one at the fusion sites with chromosomes 7 or 8, respectively. The short markers 7^{15} and 8^4 showed one signal at the centromere. (Figure 3.a).

The murine minor satellite DNA probe showed a double dot pattern only at the centromere region in the normal chromosomes and the centromeric ends of the long chromosomes 15^7 and 4^8 in all metaphases analysed (Figure 3.b). No signals were observed at the fusion sites in the long chromosomes 15^7 and 4^8. For T(4;8) also the small marker 8^4 could be examined. It showed a double dot signal as expected. No more slides of the original T(7;15) female were available for the in situ hybridization with the murine minor satellite DNA probe.

Telomere signals were seen at the ends of all chromatids including those of the long and short markers in all analysed metaphases (30 to 50) by changing the focus appropriately (Figure 3.).

Discussion

This paper is the first to describe a mouse stock with 38 chromosomes derived from a reciprocal translocation after loss of the small marker chromosome. The reciprocal translocation T(7;15) showed breaks just below the centromere of chromosome 7 and at the distal telomeric end of chromosome 15. The mice with 38 chromosomes are nullisomic for the centromere of chromosome 7 and the proximal and distal telomeres of chromosome 7 and 15, respectively.

Translocations with one break near the centromere and the other break near the distal telomere resulting in one small and one long chromosome were called c/t-type translocations (Cacheiro et al, 1974). Generally, the heterozygous males are sterile while the heterozygous females show reduced fertility (Searle, 1974). The translocation T(4;8) studied here followed the same general pattern. Unbalanced viable offspring tend to occur among progeny of c/t type translocations females rather than males (Eicher, 1973). Until now only a few c/t type translocations are known that generated sub-fertile male translocation heterozygotes, *eg* T6Ca, T31H and T70H (Beechey et al., 1980; De Boer, 1976; Eicher, 1973; Searle et al., 1971). Tertiary trisomic males are often sterile and the females show variable fertility as reported for T6Ca, T32H, T38H, T158H and T194H (Beechey and Searle, 1987; Beechey et al., 1980; Searle et al., 1983; Cattanach, 1967; Lyon and Meredith, 1966). Only in the T70H subfertile tertiary trisomics of both sexes were found (De Boer, 1973;

De Boer and Groen, 1974). The tertiary monosomic males were sterile and the females showed variable fertility in T194H and in T31H (Beechey et al., 1980; Lyon and Meredith, 1966).

In the case of T(7;15) the original female carrier and the Ms(15^7) male and female offspring were semisterile. Ts(7^{15}) and T(7;15) translocation carriers have not been mated. However, the similar testis weight/body weight ratios of the T(7;15), the 9 Ts(7^{15}) males and the Ms(715) males suggest that they were semisterile as well. The Ms (7^{15}) males had an average litter size of 4.5, when outcrossed, and 3.0, when crossed *inter se*. These litter sizes are nearly identical to the theoretically expected litter sizes for outcross of 4.3 or *inter se* cross of 3.4.

The only other fertile monosomics of both sexes occured spontaneouly in a mouse stock derived as recombination product in a pericentric inversion of Rb(6;15)1Ald with breaks in bands 6A2 and 15F2. The new stock had 39 chromosomes with a long marker chromosome 15^6 and deficient for the small segments of chromosome 6 proximal to the break point and for chromosome 15 distal to the breakpoint (Beechey and De Boer, 1983). Among the offspring of monosomic mice crossed *inter se* De Boer also found homozygous nullisomic mice with 38 chromosomes, but these mice were sterile and runted (De Boer, personal communication).

In agreement with other c/t type translocations which show preferably chain configurations and only a few ring configurations the heterozygous males from the T(7;15) and T(4;8) showed only chain and no ring configurations at diakinesis-metaphase I. In the T(7;15) and the Ts(7^{15}) males the small translocation chromosome did not participate in crossing over at all and stayed as an univalent often being lost due to the preparation procedure. The constitutional univalency of chromosome 7^{15} in spermatocytes could explain its missegregation if it also occured in oocytes. In T(4;8) males only about half the metaphase I cells showed univalency of the small marker and until now no aneuploid progeny were found in the T(4;8) line.

Among the 15 offspring of the T(7;15) female there were only 20% balanced males (1 reciprocal translocation carrier and 2 normals) but 80% aneuploids (9 trisomics and 3 monosomics) demonstrating a preferential meiotic missegregation of the small marker chromosome 7^{15} during meiosis of the original carrier female. T(7;15) resembled T31H and T194H in the fact that heterozygous females generated three times as many tertiary trisomic as teritary monosomic males. It is at variance to T6Ca for which 16% trisomics have been reported depending on the genetic background (Eicher, 1973; Baranov and Dyban 1972) while 60% trisomics occured in T(7;15).

Among the 20 offspring of *inter se* crosses of Ms(7^{15}) animals the segregation pattern was as expected for independent distribution of the chromosomes, *ie* 50% homozygotes had 38 or 40 chromosomes and 50% heterozygotes had 39 chromosomes. The homozygous mice with 38 chromosomes showed a normal phenotype and were of normal weight at weaning. Their litter size in outcrosses was almost identical to that of chromosomally normal (102/ElxC3H/El)F_1

animals and only slightly lower in *inter se* crosses, which may be due an inbreeding effect.

In the FISH analysis the small translocation chromosomes 7^{15} and 8^{4} showed one hybridization signal with the major gamma satellite DNA probe, as well as four signals with the telomere probe. This observation demonstrates that these small markers contained pericentric heterochromatin and had intact telomeres. The long marker chromosomes showed normal telomere labelling at both ends of the chromosomes and no signals at the fusion sites. With the major gamma satellite DNA probe there were two signals in the long marker chromosomes 15^{7} and 4^{8}, one at the centromere of chromosome 15 and 4 and the other at the fusion sites with chromosomes 7 and 8, respectively, indicating that the breakpoints are located within the pericentric heterochromatic block. The minor probe showed only double dot signals at the centromeres of the long chromosomes 15^{7} and 4^{8} and not at the fusion sites which suggests that the breakpoints in chromosomes 7 and 8 are located below the centromeres. This was confirmed by the signal observed in the small translocation chromosome 8^{4}. Unfortunately, the small chromosome 7^{15} could not be analysed with the minor satellite DNA probe. However, it can be assumed by analogy to the results with T(4;8) that it would have shown a signal.

Broccoli et al. (1990) found that the pmR150 minor satellite DNA probe is present in the T199H translocation at the fusion site of the long marker 10^{13}. The Y chromosome is not labelled with the pmR150 probe in contrast to the pmKC104 probe used in the present experiments which labelled all chromosomes. Therefore, it is likely that the pmKC104 is more specific for the centromere. The labelling patterns in both translocations analysed here suggest that the large marker chromosomes 15^{7} and 4^{8} carry only one centromere. Consequently, the small markers 7^{15} and 8^{4} were intact chromosomes containing centromeres and telomeres plus a fraction of pericentric heterochromatin.

It was possible to separate the long marker chromosome 15^{7} from the other mouse chromosomes by flow sorting (Miller, pers. communication). The proportional length of the two involved chromosomes 7 and 15 is 5.19% and 4.05% of the haploid genome, respectively (Evans, 1989). The proportional length of the long marker 15^{7} would be close to 9% because only the proximal telomere and the centromere of chromosome 7 plus the telomere of chromosome 15 are lost. Therefore, chromosome 15^{7} is distincly longer than chromosome 1 with a proportional length of 7.2%. From the flow diagrams the amount of lost chromosomal material was estimated to be between 0.6 and 1.4% of the haploid genome (Miller, pers. communication). It has been stated that the loss of autosomes up 2% of the haploid autosomal genome may be compatible with postnatal survival to maturity (Kirk and Searle, 1988). In the present case the loss is also compatible with full fertility and does not impair the health or phenotype of the animals which indicates that no vital genes are missing in the homozygous nullisomic mice.

The development of a homozygous mouse stock with 38 chromosomes constitutes a laboratory example for one step in the evolution of karyotypes. Generally, tandem fusions

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are rare events during evolution (Schubert and Rieger, 1992). For the laboratory mouse, the house mouse and other mouse species the most frequent deviations in chromosome numbers occured through Robertsonian fusions (Adolph and Klein, 1981; Schubert et al., 1992; Searle, 1989) but for the evolution of the Indian muntiac and the cotton rats tandem fusions have played an important role (Elder and Hsu, 1988). The animals nullisomic for chromosome 7^{15} are fully fertile and would therefore have a good chance to establish a stable chromosome number polymorphisms if they had occured in a wild population.

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Legends to Figures

Figure 1

Mating scheme of T(7;15). Circles represent females and squares represent males. Numbers below circles and squares indicate the number of progeny with the respective karyotype.

Figure 2

G-banded translocation chromosomes of T(7;15) and T(4;8). The order of the chromosome presentation is 7^{15}, 15,15^{7},7 and 8^{4},4,4^{8},8 .

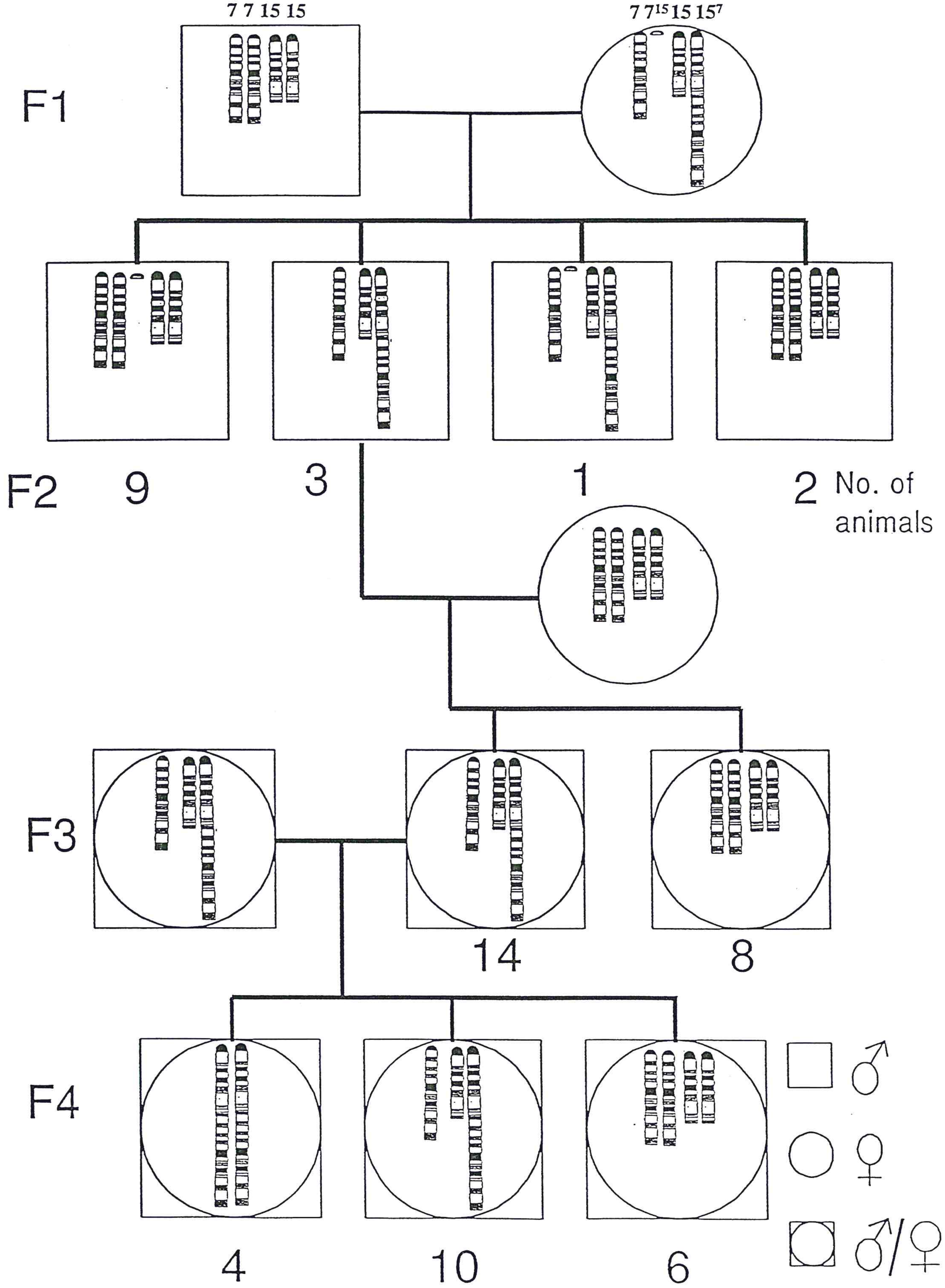
Figure 3

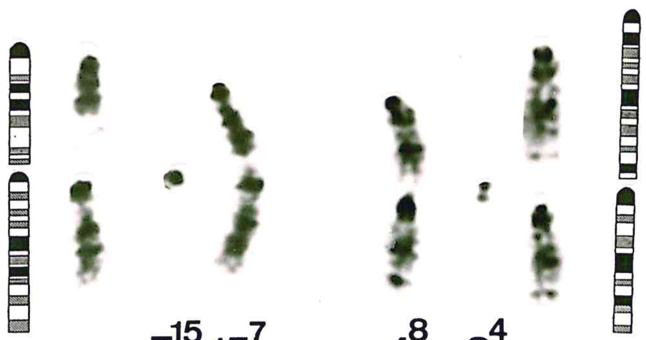
Examples of fluorescent in situ hybridization (FISH). the upper row shows T(7;15) cells, the lower row shows (T4:8) cells.

a) FISH signals with the major satellite DNA probe in the translocation chromosomes. The propidiumiodide staining on the short marker is overlapped by the yellow-green fluorescence of the major gamma satellite DNA probe.

b) FISH signals with the minor satellite DNA probe in the translocation chromosomes.

c) FISH signals with the telomere DNA probe in the translocation chromosomes


7 7 15 15
7 7^15 15 15^7
F1
F2
9
3
1
2
No. of animals
F3
14
8
F4
4
10
6
♂
♀
♂/♀


15
7
7^{15} 15^{7}
4^{8} 8^{4}
4
8

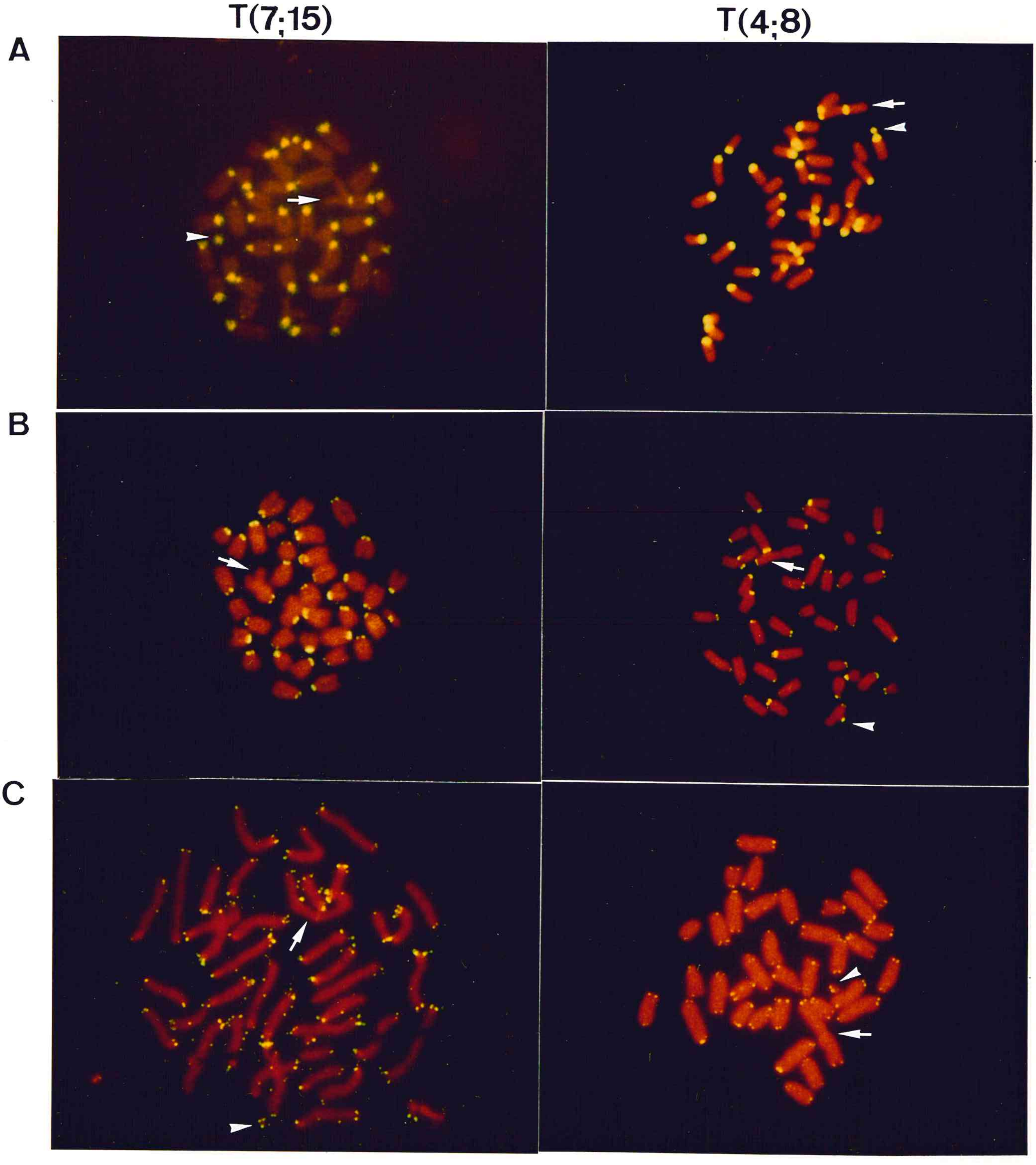

T(7;15)
T(4;8)
A
B
C

Table 1: Mean testis weight/body weight ratios for males derived from the translocations T(7;15) and T(4;8) compared to chromosomally normal males from the same stock.

Testis weight/ Body weight	T(7;15)				T(4;8)	
	$Ms(7^{15})$	$Ts(7^{15})$	T(7;15)	++	T(4;8)	++
Mean ± SD	3.0±0.4*	2.9±0.4*	3.23*	3.7±0.4	51.8±10.6*	93.0±9.3
No of animals	7	9	1	10	8	11

*p<5% (Students t-test, compared to the normal males).

$Ms(7^{15})$ = Monosomic males: 2n = 19 (-7^{15})

$Ts(7^{15})$ = Trisomic males: 2n = 21 ($+7^{15}$)

T(7;15) = Balanced heterozygote male: 2n = 20

T(4;8) = Balanced heterozygote males: 2n = 20

++ = chromosomally normal males of the same stock: 2n = 20.

Table 2: Meiotic configurations at diakinesis-metaphase I of the male progeny obtained from the original translocation carrier females

Males	No of animals	Total No of cells analysed	Number of meiotic metaphase I cells with				
			20II	20II+I	CIV	CIII	CIII+I
T(7;15)	1	25				7	18
Ms(7^{15})	3	75				75	
Ts(7^{15})	9	217	39	178			
++	2	50	50				
T(4;8)	5	125	2		69		54
++	4	100	100				

Footnotes to Tables 2:

20II = 20 bivalents

20II+I = 20 bivalents plus small univalent

CIV = chain quadrivalent

CIII = chain trivalent

CIII+I = chain trivalent plus small univalent

Ms(7^{15}) = Monosomic males: 2n = 19 (-7^{15})

Ts(7^{15}) = Trisomic males: 2n = 21 ($+7^{15}$)

T(7;15) = Balanced heterozygote male: 2n = 20

T(4;8) = Balanced heterozygote males: 2n = 20

++ = chromosomally normal males of the same stock: 2n = 20.

Table 3: Mean litter sizes of the T(7;15) progeny compared to the mean litter size of normal (102/El x C3H/El)F_1 mice

Crosses male	x	female	No. of matings	No. of litters	Litter size mean±SEM
hybrid	x	hybrid	3	9	8.6 ± 0.7
hybrid	x	$7,7^{15},15,15^{7}$	1	7	4.9 ±0.6
$7,15,15^{7}$	x	hybrid	3	20	4.5 ± 0.4
$7,15,15^{7}$	x	$7,15,15^{7}$	1	7	3.0 ± 0.2
hybrid	x	$15^{7},15^{7}$	1	2	8.5 ± 0.5
$15^{7},15^{7}$	x	$15^{7},15^{7}$	2	7	7.0 ± 0.8

hybrid = (102/El x C3H/El)F_1 animals (2n = 40)

$7,7^{15},15,15^{7}$ = balanced heterozygous animal (2n = 40)

$7,15,15^{7}$ = monosomic animals (2n = 39)

$15^{7},15^{7}$ = nullisomic animals (2n = 38)