DOMINANT X-CHROMOSOME NONDISJUNCTION MUTANTS OF *CAENORHABDITIS ELEGANS*[1]

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ABSTRACT

Eight dominant X-chromosome nondisjunction mutants have been identified and characterized. Hermaphrodites (XX) heterozygous for any one of the mutations produce 20–35% male (XO) self-progeny compared with the wild-type frequency of 0.2%. Seven of the eight mutants carry X-autosome translocations. Three of these, represented by *mnT2*, involve linkage group (LG) II and show severe crossover suppression for X-linked markers. The two half-translocations comprising *mnT2* are separable and of very unequal size. The smaller one includes the left tip of X and the right end of LGII and can exist as a free duplication, being present in addition to the normal chromosome complement, in either hermaphrodites or males; it has no effect on X nondisjunction. The reciprocal half-translocation of *mnT2* includes the bulk of both LGII and X chromosomes; it disjoins regularly from a normal LGII and confers the property of X-chromosome nondisjunction. A fourth translocation, *mnT10(V;X)*, is also reciprocal and consists of half-translocations that recombine with *V* and X, respectively. Either half-translocation of *mnT10* can exist in heterozygous form in the absence of the other to give heterozygous duplication-deficiency animals; the property of X-chromosome nondisjunction is conferred, in homozygotes as well as heterozygotes, solely by one of the half-translocations, which is deficient for the left tip of the X. The final three translocations have X breakpoints near the right end of X and autosomal breakpoints near the right end of LGIV, the left end of LGV and the right end of LGI, respectively. All three are homozygous inviable. Males hemizygous for the X portion of any of the seven translocations are viable and fertile. The final mutant, *mn164*, maps as a point at or near the left tip of the X and causes X-chromosome nondisjunction in both heterozygotes and homozygotes. In heterozygotes, *mn164* promotes equational nondisjunction of itself but not its wild-type allele. The mutants are discussed in light of the holocentric nature of the *C. elegans* chromosomes. It is proposed that the left end of the X chromosome plays a critical structural role in the segregation of X chromosomes during meiosis in XX animals.

MEIOTIC nondisjunction of the X chromosome is easy to monitor in the small free-living nematode *Caenorhabditis elegans*. *C. elegans* normally reproduces as a self-fertilizing hermaphrodite, which has two X chromosomes per cell and five pairs of autosomes (NIGON 1949). Loss of an X chromosome

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from either sperm or ovum through meiotic nondisjunction leads to the production of an animal with just one X chromosome per cell (and five pairs of autosomes), which is male and morphologically quite distinct from the hermaphrodite. Males normally arise spontaneously among the self-progeny of hermaphrodites at a frequency of about 0.2% (HODGKIN, HORVITZ and BRENNER 1979), but mutations in ten genes have been described by HODGKIN, HORVITZ and BRENNER (1979) that lead to a higher incidence of XO male self-progeny, ranging from 2–35%, depending on the mutation. The mutations are all recessive, and only one is X linked. They also increase, through the generation of diplo-X gametes, the incidence of 3X hermaphrodite self-progeny, which are shorter and less fertile than 2X hermaphrodites.

In this paper we report on the identification and characterization of a new set of mutants that show increased meiotic nondisjunction of the X chromosome and, hence, increased incidence of XO male self-progeny. The mutations differ from the set studied by HODGKIN, HORVITZ and BRENNER (1979) in that they are all dominant. The mutants are of interest, first, because they bear on the nature of meiosis in *C. elegans*, an organism of increasing genetic interest (BRENNER 1974; HERMAN and HORVITZ 1980) and, second, because they may find practical uses in future genetic work, e.g., some of the mutants show reduced X-chromosome crossing over and may be useful as balancers of X-linked deficiencies and lethal mutations and some of the mutants carry translocations having separable elements that could serve as sources of chromosome duplications and deficiencies.

Other dominant X-chromosome nondisjunction mutants of *C. elegans* have been identified. BEGUET (1978) described an autosomal dominant mutant of the Bergerac variety that gives about 20% male self-progeny when heterozygous or homozygous. The mutation appeared to be unlinked to an X-linked *dpy* marker. P. DEAK and A. FODOR (personal communication) have identified and characterized a translocation, *szT1(I;X)*, which when heterozygous promotes the production of 8–20% male self-progeny and suppresses crossing over along much of the X map. Heterozygosity for a *II*-X translocation described by HERMAN (1978) gives about 3% male self-progeny.

MATERIALS AND METHODS

Strains, growth and nomenclature: The genes used in this study and their linkage relationships are shown in Figure 1, which was derived from the current *C. elegans* genetic map prepared by D. RIDDLE and M. SWANSON of the Caenorhabditis Genetics Center (CGC), Columbia, MO. The allele numbers of the mutant genes studied are given in BRENNER'S (1974) Table 4, with the following exceptions: *dpy-4(e1166) IV*, *unc-60(e677) V*, *unc-23(e324) V*, *unc-76(e911) V* and *unc-3(e151)* X; *him-1(e879) I*, *him-6(e1423) IV* and *him-5(e1467) V* (HODGKIN, HORVITZ and BRENNER 1979); *unc-59(e1005) I* and *unc-85(e1414) II* (HORVITZ and SULSTON 1980); *rol-5(sc13) II* and *sqt-2(sc3) II* (COX *et al.* 1980); and *unc-78(e1217)* X (WATERSTON, THOMSON and BRENNER 1980). All mutants except *rol-5* and *sqt-2*, which were obtained from R. EDGAR, were obtained from the Cambridge collection (BRENNER 1974), in some instances via the CGC. N2 (wild type) and mutant strains, all the Bristol variety, were grown at 20° by the methods of BRENNER (1974). Our genetic nomenclature follows the guidelines of HORVITZ *et al.* (1979).

Isolation of dominant X-nondisjunction mutants: All of the dominant X-nondisjunction mutants were recovered incidentally in screenings for other classes of mutants. They were picked on the

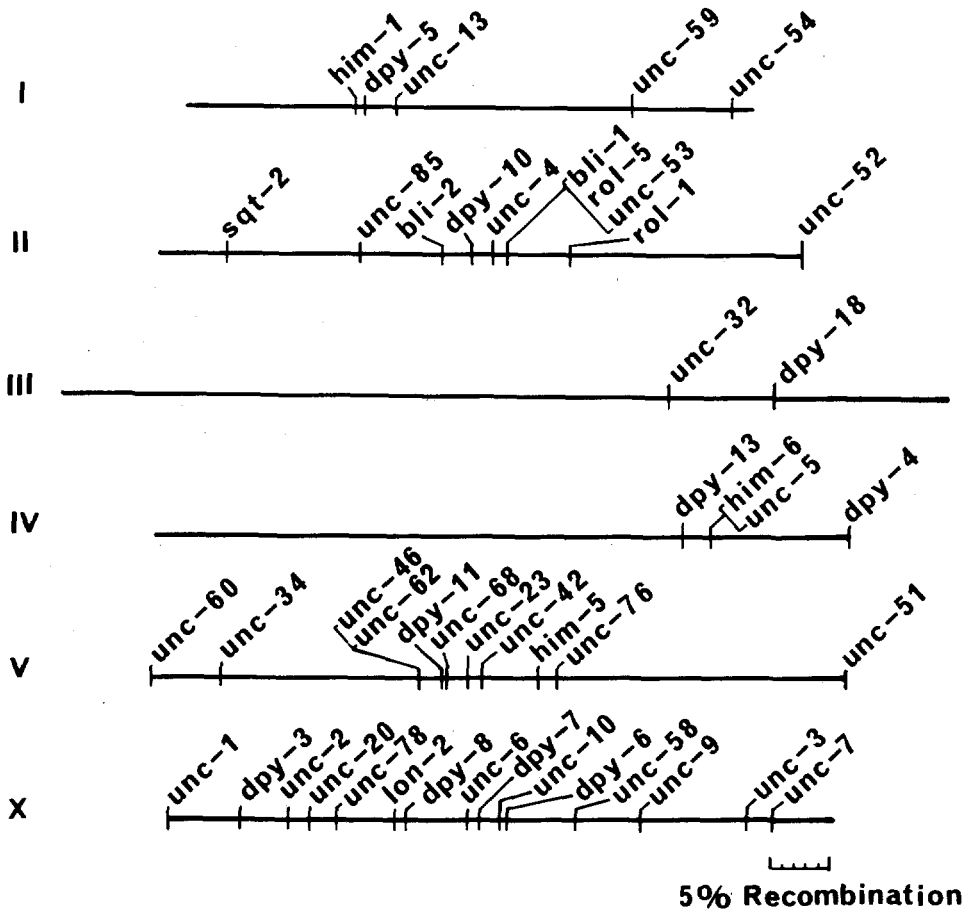

FIGURE 1.—A genetic map of *C. elegans* showing only loci used in this work.

basis of giving high frequencies of male self-progeny (Him). Whenever this trait was being assessed, hermaphrodite larvae were picked to ensure that all progeny were self-progeny. The translocation mutant *mnT10(V;X)* was first picked as a single hermaphrodite from the F_2 brood of an N2 animal treated with ethyl methanesulfonate by the procedure of BRENNER (1974). All of the other mutants were first picked as single hermaphrodites from F_1 broods of X-irradiated parents (7500 r at 450 r/min) during searches for dominant crossover suppressor mutations (HERMAN 1978). *mnT3(II;X)*, *mnT7(IV;X)*, *mnT8(V;X)*, *mnT9(I;X)* and *mn164* were independent mutants picked as self-progeny of irradiated hermaphrodites bearing LGIII visible markers; *mmT2(II;X)* was found among the self-progeny of an irradiated hermaphrodite bearing LGI markers; *mnT6(II;X)* was found among the cross-progeny of an irradiated male and unirradiated hermaphrodite, both bearing LGIII markers. All of the visible markers that were originally present in mutant strains were subsequently removed.

Outcrosses were accomplished by mating male self-progeny of a mutant strain with a recessive visible mutant hermaphrodite and picking wild-type hermaphrodite cross-progeny to check for the presence of the Him property. We thus required that fertile males be capable of inheriting the mutation and of transmitting it to their progeny. The linkage relationship between the dominant Him-conferring mutation and the visible marker was determined by picking individual visible mutant segregants and checking the frequency at which they segregated male self-progeny. In this way, all of the dominant X-nondisjunction mutants were shown to be X linked, and heterozygous stocks in which each mutation was balanced by a closely linked visible marker in *trans* were

constructed. Such stocks segregated both visible mutant males and wild-type males, and, as expected, most of the wild-type males transmitted the Him trait to their hermaphrodite progeny. The mutant-bearing males were *XO* males, as opposed to *XX* transformed males (KLASS, WOLF and HIRSH 1976; HODGKIN and BRENNER 1977), because they sired both hermaphrodite and male progeny.

Genetic techniques: Mating, counting and mapping procedures were as described by HERMAN (1978). Animals whose progeny were to be scored were transferred daily, and full broods were scored. The wild-type category, abbreviated W in the tables, sometimes included small animals, at least some of which were triplo-X (HODGKIN, HORVITZ and BRENNER 1979). The recombination frequency, *p*, was as defined by BRENNER (1974), with appropriate account taken of unusual markers, such as *sqt-2* (COX *et al.* 1980).

An mnT2 unc-3 *recombinant*: An Unc non-Dpy segregant from a *dpy-3 unc-3/mnT2* hermaphrodite was mated with *mnDp1(X;V)/+; unc-7/0* males (HERMAN, ALBERTSON and BRENNER 1976). Among the wild-type hermaphrodite cross-progeny were found *unc-7/mnT2 unc-3* hermaphrodites, which segregated Unc-7 and Unc-3 male self-progeny. Because recombination between *mnT2* and a normal X chromosome is rare (see RESULTS), we confirmed that the *mnT2 unc-3* recombinant behaved in the same way as *mnT2* with respect to the following properties. First, we demonstrated that *mnT2 unc-3* suppressed crossing over on the X chromosome. This was shown by scoring the self-progeny of *lon-2 unc-7/mnT2 unc-3* hermaphrodites, which were constructed by mating *mnDp1/+; lon-2 unc-7/0* males with *unc-7/mnT2 unc-3* hermaphrodites. Second, we showed that *mnT2 unc-3* behaved as a *II-X* translocation by scoring the self-progeny of *dpy-10/mnT2 unc-3* hermaphrodites, which were constructed by mating *dpy-10/+* males with *unc-7/mnT2 unc-3* hermaphrodites. And third, we showed that *mnT2 unc-3* was subject to segregational loss of an essential portion of the X chromosome: *mnDp1/+; mnT2 unc-3* males were crossed with *dpy-10; unc-3* hermaphrodites, and among the cross-progeny hermaphrodites, animals were found that segregated Dpy Unc male self-progeny but extremely few Unc non-Dpy male self-progeny.

RESULTS

The isolation and initial characterization of the mutants as X linked, dominant X-chromosome nondisjunction mutants is described in MATERIALS AND METHODS. The following results were obtained with stocks that had been established after at least three outcrosses, as described in MATERIALS AND METHODS.

mn164: The three-factor crosses given in Table 1 show that the Him-conferring mutation *mn164* maps very near the left-most marker on the X-linkage map, *unc-1* (see Figure 1 for map). Because *unc-1* is slightly semidominant to *unc-1* $^{+}$, we have preferred to use the closely linked marker *dpy-3* to tag the *mn164*$^{+}$ chromosome in a heterozygote: *mn164/dpy-3* hermaphrodites segregated 25% males, both Dpy and wild type, among their self-progeny (1858 total progeny scored). Among the wild-type hermaphrodite progeny of *dpy-3/mn164*, about one-third (17 of 52) did not segregate Dpy self-progeny. These animals were *mn164* homozygotes. Homozygous *mn164* hermaphrodites segregated 19% male self-progeny (among 1214 total progeny scored).

The *mn164* mutation does not appear to involve a gross chromosomal rearrangement. We looked for psuedolinkage of *dpy-3* X to *unc-13 I*, *unc-4 II*, *unc-32 III*, *unc-5 IV* or *unc-42 V* in *mn164* heterozygotes as evidence for the involvement of a translocation, but the result was that all pairs of markers assorted independently. The Him trait has invariably been associated with a homozygous viable X chromosome, unlike some other dominant X nondisjunction mutants. The *mn164*-bearing chromosome recombined readily with a normal homologue: among the progeny of *mn164/dpy-3 unc-3*, 122 of 535 hermaphrodites were

TABLE 1

Three-factor mapping of dominant Him *mutants*

Parental genotype	Phenotype of selected recombinant	Proportion of recombinants with Him phenotype
mn164/dpy-3 unc-3	Dpy	0/8
	Unc	9/9
mn164/dpy-3 unc-2	Dpy	0/3
	Unc	4/4
mn164/unc-1 dpy-3	Dpy	3/3
	Unc	0/4
mnT2/dpy-3 unc-3	Dpy	0/17
	Unc	13/13
mnT2/dpy-10 unc-53	Dpy	13/14
	Unc	0/6
mnT2/sqt-2 unc-4	Rol Unc[a]	0/7
mnT2/dpy-10 unc-52	Dpy	0/6
mnT2/unc-4 rol-1	Unc	0/15
mnT10(X)/dpy-3 unc-6	Dpy	0/21
	Unc	4/4
mnT10(X)/dpy-7 unc-3	Dpy	0/52
	Unc	59/59
mnT7/dpy-7 unc-3	Dpy	9/9
	Unc	0/3
mnT8/dpy-7 unc-3	Dpy	2/4
	Unc	0/2
mnT9/dpy-3 unc-3	Dpy	7/7
	Unc	1/10

[a] *sqt-2/+* has a roller phenotype; *sqt-2/sqt-2* does not (COX *et al.* 1980).

recombinant (P = 0.27) and 86 of 218 males (P = 0.39) were recombinant; the normal frequency is about 0.34 (BRENNER 1974).

The crosses shown in Table 2 were conducted with the purpose of evaluating the products of oogenesis in *mn164* heterozygotes. The results show that the relative proportions of ova that were nullo-X, haplo-normal X, haplo-*mn164*, diplo-*mn164* and diplo-normal X were about 18:10–14:17:3:0, respectively. This analysis omits from consideration diplo-X ova that contain an *mn164*-bearing chromosome and a normal X; such ova, which would have been produced by reductional nondisjunction, were probably produced (based on the relatively high frequency of hermaphrodite cross-progeny from the matings given in Table 2), but we did not prove that they were. It is interesting to note that the *mn164*-bearing chromosome showed equational nondisjunction and that its homologue did not. The four recessive *him* mutations that have been tested in this respect showed reductional nondisjunction only (HODGKIN, HORVITZ and BRENNER 1979).

The *mn164*-bearing chromosome in XO males appears to behave normally during meiosis. The ratio of nullo-X to haplo-X sperm, as measured by the sex ratio of cross-progeny, was 1.04 (2385 total cross-progeny). The frequency of diplo-X sperm was shown to be about 0.003: one non-Unc-58 hermaphrodite was found among 195 non-Unc-58 progeny of matings between *him-1 I; him-5*

TABLE 2

Ova produced by mn164 heterozygotes

Parental genotypes[a]	Cross progeny frequencies					
	non-Unc-4 non-Dpy hermaphrodite	W male	Unc-1 male	Dpy male	Dpy hermaphrodite	Total animals scored
unc-4 II; unc-1/mn164 dpy-3 X ♀ ×*N2* ♂ ♂	0.48	0.18	0.14	0.17	0.03[b]	1067
	W hermaphrodite	W male	Dpy male	Dpy hermaphrodite		
unc-4 II; dpy-3/mn164 X ♀ ×*N2* ♂♂	0.50	0.40	0.10	0.00		602

[a] Hermaphrodites were mated individually with four N2 males.
[b] Many of these animals were picked and shown, by progeny testing, to be *mn164 dpy-3* homozygotes.

unc-76 V; unc-58 X hermaphrodites and *mn164/0* males. The hermaphrodites used in these matings produce substantial nullo-X ova (HODGKIN, HORVITZ and BRENNER 1979), which are the only source of non-Unc-58 cross-progeny because *unc-58* is dominant to its wild-type allele.

mnT2(II,X): To aid the reader, we state at the outset certain conclusions that will be reached about *mnT2(II;X)*. We shall conclude that it is a reciprocal transloction as diagramed in Figure 2. The two half-translocations comprising *mnT2* are called *mnT11(II;X)* and *mnDp11(II,X;f)*. We shall conclude that the dominant Him property is due solely to *mnT11*, which disjoins from LGII and is viable in the absence of *mnDp11* when a normal *II* and a normal X are present. On the other hand, we shall show that *mnDp11* in the absence of *mnT11* behaves as a free duplication, being present in addition to the normal diploid complement. The analysis that follows anticipates these conclusions only insofar as the dominant Him-conferring mutation is called *mnT2* (or, more specifically, *mnT11*) before the evidence for this conclusion is given.

The dominant Him-conferring mutation *mnT2* balances virtually any X-linked visible marker in *trans*: for example, from either *mnT2/dpy3* or *mnT2/-unc-3*, all wild-type hermaphrodite self-progeny (40 of 40 and 30 of 30, respectively) were heterozygous for the Him-conferring mutation, and almost all Dpy (60 of 60) or Unc (26 of 28) hermaphrodite self-progeny were non-Him. This result means that *mnT2* homozygotes are rare or inviable and suggests that *mnT2* suppresses crossing over. The self-progeny ratios from *mnT2/dpy-3 unc-3* animals confirm that *mnT2* suppresses crossing over: five Dpy and three Unc recombinants were found among 940 self-progeny hermaphrodites (P = 0.009), whereas the normal *dpy-3* to *unc-3* recombination distance is about 34% (BRENNER 1974).

The wild-type male (*mnT2/0*) self-progeny of *mnT2/dpy-3* hermaphrodites sire two classes of hermaphrodite cross-progeny, both of which are Him; in one class the Him-conferring mutation is coupled to an X-linked recessive lethal

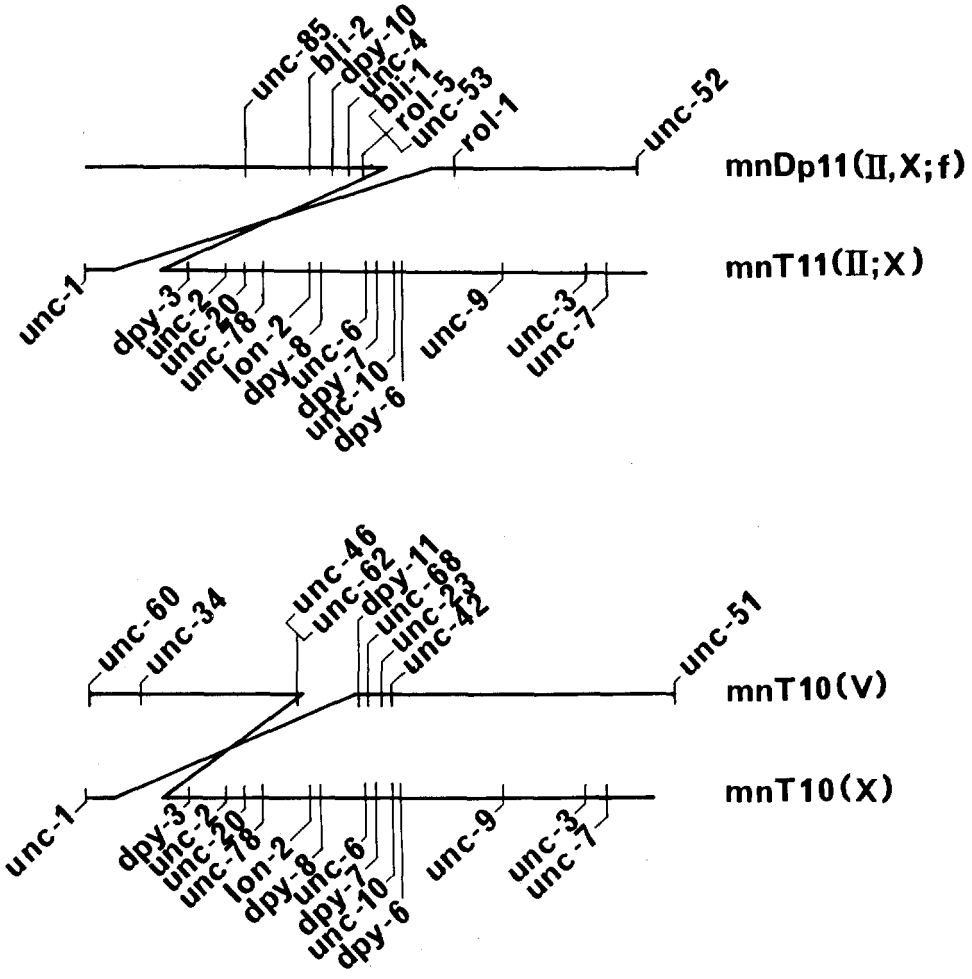

FIGURE 2.—Proposed breakpoints and rejoinings for formation of *mnT2*, which consists of *mnDp11* and *mnT11*, and for formation of *mnT10(V;X)*, which consists of *mnT10(V)* and *mnT10(X)*. All of the markers shown have been tested with respect to which element they reside on.

and in the other class it is not. For example, among wild-type hermaphrodite cross-progeny of *mnT2/0* × *dpy-8* X, about half segregated both wild-type and Dpy males, and the others segregated Dpy males only. The heterozygous X-linked lethal hermaphrodites were smaller both as larvae and as adults than their nonlethal-bearing sibs. Similar results were obtained in crosses with *dpy-3, unc-2, unc-20, unc-78, lon-2, dpy-8, unc-6, dpy-7, unc-10, dpy-6, unc-9, unc-3* and *unc-7*. The case of *unc-1* X was different, however. The recessive lethal-bearing chromosomes failed to complement *unc-1*: among the progeny of *mnT2/0* × *unc-1 dpy-8*, Unc-1 non-Dpy hermaphrodite cross-progeny were produced, and they (41 of 41) segregated Unc Dpy males but not Unc males, whereas the wild-type hermaphrodite cross-progeny (37 of 37) segregated both classes of males. We propose from these results that a portion of *mnT2*, which carried *unc-1*$^+$ and at least one X-linked essential gene and is called *mnDp11*, can be

easily lost through meiotic segregation. The remaining portion of *mnT2* is called *mnT11*. The loss of *mnDp11* is particularly apparent during male spermatogenesis: in the cross just cited, 29 of 52 hermaphrodite cross-progeny were hemizygous for *unc-1*. We have also observed such loss in hermaphrodites, however. Among 257 hermaphrodite self-progeny of *mnT2/unc-1 dpy-8* animals, for example, 12.1% were Unc-1 animals that segregated Unc Dpy males but not Unc males. Hermaphrodites deficient for *mnDp11* showed the same low frequency of recombination in the *dpy-3* to *unc-3* interval as the heterozygous *mnT2* stock from which they were derived.

The pseudolinkage results in Table 3 show that the Him-conferring mutation is associated with a translocation between linkage groups II and X; the pseudolinkage was apparent whether or not *mnDp11* was present (Table 3). Pseudolinkage of *unc-6* X to autosomal markers *dpy-5 I, dpy-18 III, dpy-13 IV* and *dpy-11 V* was also tested, with the result that all of these pairs of markers assorted independently.

It is natural to ask whether the X-linked lethal-bearing hermaphrodites (deficient for *mnDp11*) were hemizygous for any LGII genes. Table 3 shows that such animals were not hemizygous for *dpy-10*, since both *dpy-10*$^+$ and *dpy-10* genes were present in the *mnDp11*-deficient animals. Analogous crosses showed that *mnDp11*-deficient strains heterozygous for *unc-85, bli-2, unc-4, bli-1* or *unc-53* could also be constructed. On the other hand, *mnDp11*-deficient hermaphrodites heterozygous for *unc-52* could not be constructed. Complementation tests showed directly that *mnDp11*-deficient hermaphrodites were hemizygous for *unc-52*$^+$.

The behavior of *mnDp11* as a free duplication carrying *unc-52*$^+$ was established in the following way. This analysis makes use of a dominant crossover suppressor for the *dpy-10 II* to *unc-52 II* interval that maps very close to these markers and is called *C1* (HERMAN 1978). *mnT2* males were crossed with *unc-4 unc-52* hermaphrodites, and from the wild-type hermaphrodite progeny, Unc-4 self-progeny were picked. As expected, these animals (14 of 14) were non-Him (putative genotype: *unc-4 unc-52/unc-4 unc-52; mnDp11*) and segregated many paralyzed offspring (*unc-52*, which gives a paralyzed phenotype, is epistatic to *unc-4*). *C1 dpy-10 unc-52/unc-4* males were crossed with *mnDp11/unc-4 unc-52/unc-4 unc-52* hermaphrodites, and wild-type hermaphrodite progeny were picked. The genotype of these animals, which was *mnDp11/C1 dpy-10 unc-52/unc-4 unc-52*, was confirmed by the self-progeny ratios: 0.32 wild type:0.26 Unc-52:0.16 Unc-4:0.18 Dpy:0.09 Unc-52 Dpy (1121 total progeny). These progeny ratios show that the *mnDp11*-containing parent had two complete LGII chromosomes, *C1 dpy-10 unc-52* and *unc-4 unc-52*, in addition to the *unc-52*$^+$ duplication (HERMAN, MADL and KARI 1979). Furthermore, the following result showed that the duplication-bearing strain does not give viable hypoploids, containing *mnDp11* and just one LGII chromosome. In the cross already described between *C1 dpy-10 unc-52/unc-4* males and *mnDp11/unc-4 unc-52/unc-4 unc-52* hermaphrodites, among several hundred cross-progeny, no *mnDp11/C1 dpy-10 unc-52* animals, which would have been Dpy, were found. We followed the segregation of *mnDp11* in oogenesis by counting wild-type male and Unc-52 male progeny from this same cross. The results indicated that

TABLE 3

Pseudolinkage results involving mnT2

Parental genotype	Phenotypic ratios of self-progeny								Total progeny scored
	Hermaphrodites				Males				
	W	Dpy Unc	Dpy	Unc	W	Dpy Unc	Dpy	Unc	
dpy-10 II; mnT11 mnDp11; unc-6 X	0.52	0.12	0.02	0.02	0.17	0.13	0.02	0.02	329
dpy-10 II; mnT11; unc-3 X	0.51	0.13	0.02	0.02	0.00	0.28	0.00	0.04	241
unc-53 II; mnT11 mnDp11; dpy-3 X	0.51	0.11	0.00	0.00	0.24	0.14	0.00	0.00	1186

29% (279 total male progeny scored) of the ova of *mnDp11/unc-4 unc-52/unc-4 unc-52* hermaphrodites inherited *mnDp11*. Segregation of *mnDp11* in male spermatogenesis was followed in a cross of *mnDp11/C1 dpy-10 unc-52/unc-4 unc-52* males (generated by crossing *C1 dpy-10 unc-52/unc-4* males with *mnDp11/unc-4 unc-52/unc-4 unc-52* hermaphrodites) with *unc-52* hermaphrodites. The numbers of cross-progeny scored were 115 wild-type hermaphrodites (from *mnDp11*, X sperm), 195 wild-type males (from *mnDp11* sperm), and 95 Unc-52 males (from nullo-*mnDp11*, nullo-X sperm). These results indicate that *mnDp11* and X tend to segregate from each other during male spermatogenesis. This is a property of certain other free duplications (HERMAN, MADL and KARI 1979).

The following cross shows that *mnT2* males produce nullo-X, *mnDp11*-bearing sperm. Males of genotype *unc-4 unc-52 II/mnT2/0* were crossed with *unc-4 unc-52* hermaphrodites, and the numbers of cross-progeny scored were: 86 wild-type hermaphrodites (from *mnDp11*, *mnT11* sperm), 86 Unc-52 males (from nullo-*mnDp11*, nullo-*mnT11* sperm), and 110 Unc-4 males (from *mnDp11*, nullo-*mnT11* sperm).

We next show that it is possible to reconstruct the *mnT2* translocation by combining the separated half-translocations, *mnDp11* and *mnT11*. Males of genotype *mnDp11/C1 dpy-10 unc-52/unc-4 unc-52* were crossed with *mnT11/unc-1 dpy-8* hermaphrodites (which are Unc-1 and Him, yielding Unc Dpy but not Unc non-Dpy self-progeny males). Wild-type male progeny were picked and mated individually with *dpy-10; unc-7* hermaphrodites to test for production of *mnT2*-bearing hermaphrodite cross-progeny. Four of nine fertile males proved to have carried *mnT2*.

Complementation tests between *rol-1* and the *mnT11*-bearing stocks hemizygous for *unc-52*$^{+}$ were inconclusive, probably because the smallness of the animals deficient for *mnDp11* precluded full expression of the roller phenotype, which is normally manifested only in adult animals (COX *et al.* 1980). We have shown, using duplication-bearing hyperploids, however, that *mnDp11* suppresses *rol-1 II*. Males of genotype *mnDp11/C1 dpy-10 unc-52/unc-4 unc-52* were crossed with *rol-1 unc-52* hermaphrodites. Wild-type hermaphrodites were picked and allowed to self-fertilize. In those broods that contained Dpy Unc-52 animals, no Rol non-Unc-52 animals were observed, and wild-type hermaphro-

dites were picked. Some proved not to carry the *C1 dpy-10 unc-52* chromosome and were, therefore, *mnDp11/rol-1 unc-52/rol-1 unc-52*. (Because *unc-52* is epistatic to *rol-1*, we confirmed by further crosses that the *rol-1* mutation was present in this strain.) These animals were of normal size but did not roll, hence *mnDp11* suppresses *rol-1*, presumably because it carries the *rol-1*$^+$ gene. By contrast, the same kind of analysis showed that *mnDp11* does not carry *rol-5*$^+$ *II*.

We have screened 2093 progeny of *mnDp11/rol-1 unc-52/rol-1 unc-52* hermaphrodites for the appearance of Rol non-Unc-52 recombinants and found none. Such recombinants were also rare among the self-progeny of *mnT2/rol-1 unc-52* animals: one was found among 1069 offspring; by contrast, 188 Rol non-Unc-52 recombinants were found among 2493 self-progeny of *rol-1 unc-52/+ +* animals.

mnT2(II;X) generates very tight linkage between *unc-53 II* and *dpy-3* X (Table 3), which is expected because these markers normally map close to the breakpoints of the translocation, as defined by the markers carried by *mnDp11(II,X;f)*: *unc-1* X and *rol-1 II* but not *dpy-3* X or *unc-53 II*. The three-factor crosses given in Table 1 indicate that the Him trait is conferred by *mnT11*: the Him-conferring mutation mapped much closer to *dpy-3* X than to *unc-3* X and nearer to *unc-53 II* than to *dpy-10 II*.

Recombination between *mnT2* and a normal LGII homologue was not suppressed in the *sqt-2* to *unc-4* interval. A *sqt-2* heterozygote has a right-handed roller phenotype, whereas the *sqt-2* homozygote shows wild-type movement (COX *et al.* 1980). We found 44 of 93 recombinant Rol Unc hermaphrodites among the Unc and Rol Unc self-progeny of *mnT2/sqt-2 unc-4* animals (P = 0.38); by comparison, we found 110 of 302 Rol Unc recombinants among the Unc and Rol Unc self-progeny of *+ +/sqt-2 unc-4* animals (P = 0.24). Dpy and Unc recombinant self-progeny from *mnT2/dpy-10 unc-52* hermaphrodites were frequent, but as expected, they appeared to represent primarily segregational events rather than crossovers. Six of six Dpy recombinants (all non-Him) segregated about 50% Dpy Unc self-progeny, which suggests that the Dpy animals were *mnDp11/dpy-10 unc-52/dpy-10 unc-52*. Analogous results were found for 10 of 10 Unc recombinant self-progeny of *mnT2/unc-4 rol-1*.

We have looked for evidence of nondisjunction of *mnT2* and its normal LGII homologue by means of the following matings: *him-6* males were crossed with *sqt-2 II/sqt-2 mnT2/unc-6* X; *dpy-11 V* hermaphrodites. Cross-progeny (non-Dpy) should all be rollers unless a nullo-*II* sperm fertilizes a diplo-*II* ovum or a diplo-*II* sperm fertilizes a nullo-*II* ovum. HODGKIN, HORVITZ and BRENNER (1979) have shown that *him-6* animals undergo autosomal nondisjunction, generating probably about 2–3% diplosomic and 8–9% nullosomic gametes for each autosome. Among 2385 progeny of the above cross, only one exceptional animal proved to have been generated by nondisjunction in both parents: it was *sqt-2 II/sqt-2 mnT2/+* X; *dpy-11 V/+*. We conclude that *mnT2* leads to less than about 1% diplo-*II* and less than about 2% nullo-*II* ova.

To follow the disjunction of *mnT2* and the X chromosome in hermaphrodites, we have marked *mnT2* with *unc-3* X. The results of the cross shown in Table 4 show that heterozygous *mnT2* hermaphrodites produced nullo-X, *mnT2* and

TABLE 4

Ova produced by mnT2 *heterozygotes: cross-progeny from* dpy-11 V; mnT2 unc-3/unc-7 X ♀ × *N2* ♂ ♂[a]

Cross-progeny frequencies						
W hermaphrodites	Unc-3 hermaphrodites	Unc-7 hermaphrodites	W males	Unc-3 males	Unc-7 males	Total cross-progeny scored
0.45[b]	0.001	0.000	0.28	0.12	0.15	1113

[a] Hermaphrodites were mated individually with four N2 males.
[b] Fourteen of these animals were picked and progeny tested; four proved to be *mnT2 unc-3/unc-7*.

normal X ova in the proportions 28:12:15, respectively. The relatively low frequency of *mnT2*-bearing ova is expected because *mnT2* includes both *mnT11*, which disjoins from the normal *II*, and *mnDp11*; ova carrying *mnT11* alone when fertilized by nullo-X sperm will give rise to inviable zygotes. The relatively low frequency of normal X ova, however, implies that the normal X tends to be lost. This is expected because HODGKIN (1980) has shown that an unpaired X chromosome in XO animals made hermaphroditic by the mutation *her-1* tends to be lost during meiosis. Among the wild-type hermaphrodite cross-progeny, four of 14 proved by progeny testing to be *mnT2 unc-3/unc-7*, which means that they were derived from diplo-X ova produced by reductional nondisjunction. No diplo-X ova with two normal X chromosomes, which would have been represented by Unc-7 hermaphrodite cross-progeny, were identified. No evidence for diplo-*mnT2* ova was obtained either (the one Unc-3 hermaphrodite cross-progeny in Table 4 may have carried an *unc-3* recombinant chromosome), but such ova would have generated animals with three copies of much of LGII, which might be lethal; therefore, we cannot say that diplo-*mnT2* ova were not produced. Many of the wild-type hermaphrodite cross-progeny classified in Table 4 were small animals, many of which were probably triplo-X (HODGKIN, HORVITZ and BRENNER 1979) or carried *mnT11* but not *mnDp11*, as already discussed.

Only 1% of the self-progeny of *unc-7/mnT2 unc-3* hermaphrodites (671 total progeny scored) were Unc-3 hermaphrodites, which indicates that homozygous *mnT2* hermaphrodites were rarely produced. Some of the rare Unc-3 hermaphrodites appeared to carry a recombinant *unc-3* chromosome, segregating non-Him progeny. A few individuals have been found, however, that appeared to be *mnT2 unc-3* homozygotes; these animals grew slowly, gave very small viable broods and many unhatched eggs, were Him, and segregated hermaphrodite progeny that were all Him.

mnT3(II;X) *and* mnT6(II;X): two other dominant Him mutants appear to be similar to *mnT2(II;X)*, although we have not analyzed them in nearly as much detail as *mnT2(II;X)*. For each mutant, heterozygotes segregated about 37% males, including both mutant and wild-type males. Pseudolinkage data showed that the Him trait in each mutant was associated with a *II*-X translocation. Each translocation showed greatly suppressed recombination with a normal X hom-

ologue: *mnT3/dpy-3 unc-3* gave 1 Dpy and 3 Unc recombinants among 234 self-progeny hermaphrodites ($p = 0.02$), and *mnT6/dpy-3 unc-3* gave 0 Dpy and 0 Unc recombinants among 1177 self-progeny hermaphrodites. For both mutants, homozygous translocation hermaphrodites were rare or inviable. And in both cases, translocation males produced hermaphrodite cross-progeny that were hemizygous for *unc-1*$^+$, an essential X gene and *unc-52*$^+$, and these animals were small. The ova of *mnT3*/X hermaphrodites were analyzed by crosses analogous to those shown in Table 5, with results almost identical with those found for *mnT2*.

mnT10(V;X): To aid the reader, we begin dicussion of *mnT10(V;X)* by stating some conclusions that will be made: we shall conclude that *mnT10(V;X)* is a reciprocal translocation with separable half-translocations designated *mnT10(V)* and *mnT10(X)*, as diagramed in Figure 2, and we shall conclude that the Him property is due solely to *mnT10(X)*, whether heterozygous with a normal X chromosome or homozygous. We anticipate these conclusions in the following presentation only in our use of *mnT10(X)* to denote the Him-conferring mutation before the evidence for doing so is presented.

The dominant Him-conferring mutation *mnT10(X)* maps near *dpy-3* X. Virtually all fertile wild-type hermaphrodite self-progeny of *mnT10(X)/dpy-3* were Him (284 of 284), and virtually all fertile Dpy hermaphrodite self-progeny were non-Him (278 of 278). By contrast, only 45 of 52 Lon self-progeny of *mnT10(X)/lon-2* were non-Him.

The *mnT10(X)/dpy-3* hermaphrodites fell into two classes, based on their self-progeny ratios. One class segregated both wild-type and Dpy males; the other class segregated Dpy males only, indicating that *mnT10(X)* was closely coupled to an X-linked hemizygous lethal mutation. The lethal-bearing hermaphrodites arose frequently as self-progeny from the other class of heterozygote, but the reverse did not occur. The lethal-bearing class of hermaphrodite also arose frequently from crosses between *mnT10(X)* males and *dpy-3* hermaphrodites. We have tested for hemizygosity of X-linked visible markers in the lethal-bearing hermaphrodites. The following markers could be made heterozygous in lethal-bearing animals: *dpy-3, unc-2, unc-20, unc-78, lon-2, dpy-8, unc-6, dpy-7, unc-10, dpy-6, unc-9, unc-3* and *unc-7*. The one exceptional marker found was *unc-1*, which was hemizygous in lethal-bearing animals: among the hermaphrodite cross-progeny of *mnT10(X)/0* × *unc-1 dpy-8*, Unc-1 non-Dpy animals were frequent, and five of five segregated Unc Dpy males but virtually no Unc non-Dpy males; five of five wild-type hermaphrodite cross-progeny, by contrast, segregated many wild-type males as well as Unc Dpy males. These results are then similar to what was found for *mnT2(II;X)*; the obvious suggestion is that loss of a half-translocation—to be called *mnT10(V)*—that carries *unc-1*$^+$ and at least one essential X-linked gene, is occurring by meiotic segregation; thus, *mnT10(X)/0* males must also carry *mnT10(V)* to be viable. We found no pseudolinkage of *dpy-3* to *unc-13 I, unc-4 II, unc-32 III, unc-5 IV* or *unc-42 V* by looking at hermaphrodite self-progeny of *mnT10(V;X)* heterozygotes. A kind of pseudolinkage was found, however, by looking at the male self-progeny of *mnT10(V;X)* heterozygotes. The method is illustrated as follows:

TABLE 5

Identifying LGV *markers on* mnT10(V) *and* mnT10(X)

Parental genotype	Frequencies of self-progeny								Total animals scored
	Hermaphrodites				Males				
	W	Dpy	Unc	Dpy Unc	W	Dpy	Unc	Dpy Unc	
A. *mnT10(V)/unc-42; mnT10(X)/dpy-3*	0.528	0.054	0.107	0.074	0.179	0.016	0.000	0.042	447
B. *unc-42/+; mnT10(X)/dpy-3*	0.448	0.224	0.146	0.086	0.000	0.078	0.000	0.018	603
C. *unc-60/+; mnT10(X)/dpy-3*	0.560	0.225	0.000	0.108	0.000	0.080	0.000	0.027	623

mnT10(V;X) males were crossed with *unc-42 V; dpy-3* X hermaphrodites; the resulting wild-type hermaphrodite progeny that segregated wild-type males also segregated Unc Dpy males but no Unc non-Dpy males; see the self-progeny ratios of genotype A in Table 5. It follows that *unc-42*$^+$ *V* is coupled to an essential part of the X chromosome. It is not coupled to *dpy-3*$^+$, which is on *mnT10(X)*, however, because Unc non-Dpy hermaphrodites were frequent; therefore, *unc-42*$^+$ must be coupled to that part of X that carries *unc-1*$^+$, *viz. mnT10(V)*.

We now show that *mnT10(V;X)* can be reconstituted from separated *mnT10(V)* and *mnT10(X)* elements. Males carrying both *mnT10(V)* and *mnT10(X)*, picked as wild-type male self-progeny of *mnT10(V;X)/dpy-3* hermaphrodites, were mated with *mnT10(X) unc-6/dpy-3 unc-6* hermaphrodites. The latter animals segregated Dpy Unc male self-progeny but no Unc non-Dpy male self-progeny, owing to the absence of *mnT10(V)*. About 9% (36 of 391) of the progeny (including both cross-progeny and self-progeny) of the mated parents were Unc non-Dpy males; these animals must have received *mnT10(V)* from the male parent and *mnT10(X) unc-6* from the hermaphrodite parent.

A majority of the Dpy self-progeny of *mnT10(V)/unc-42; mnT10(X)/dpy-3* animals were slow growing and sickly and gave small broods of self-progeny, a majority of which suffered from the same defects. Since these animals must have been largely *mnT10(V)/unc-42; dpy-3/dpy-3*, it appears that *mnT10(V)* in the absence of *mnT10(X)* is responsible for this phenotype. This effect was not specific to the *dpy-3* marker, since the same effect was noted (although it was not as marked) when *lon-2* was substituted for *dpy-3*. Furthermore, as expected, the Dpy offspring of *unc-42/+; dpy-3/mnT10(X)*—see self-progeny of genotype B in Table 5—were normal.

The absence of the Unc hermaphrodites among the self-progeny of *unc-60/+; dpy-3/mnT10(X)*—genotype C in Table 5—indicates that *unc-60*$^+$ is coupled to *dpy-3*$^+$ and hence to *mnT10(X)*; compare rows B and C in Table 5. Results for *unc-32 V*, *unc-46 V* and *unc-62 V* were strictly analogous to those for *unc-60 V*, whereas results for *unc-68*, *unc-23* and *dpy-11* (using *unc-2* X rather than *dpy-3* as X-linked balancer of *mnT10(X)* in the case of the *dpy-11* test) were strictly analogous to those of *unc-42*. In summary, the LGV markers

unc-60$^+$, *unc-34*$^+$, *unc-46*$^+$ and *unc-62*$^+$ are coupled to *dpy-3*$^+$ and *mnT10(X)*, and the markers *dpy-11*$^+$, *unc-68*$^+$, *unc-23*$^+$ and *unc-42*$^+$ are coupled to *mnT10(V)*. We have also shown that the *mnT10(V)*-bearing chromosome fails to complement *unc-34*, *unc-46* and *unc-62*; for example, *mnT10(V)/+; mnT10(X)/0* males mated with *unc-46* hermaphrodites produce Unc-46 male cross-progeny, genotype *mnT10(V)/unc-46; +/O*. As expected, these animals were sickly (but readily recognized). We were unable to show lack of complementation between *mnT10(V)* and *unc-60*, presumably because *mnT10(V)/unc-60; +/0* animals are inviable; *unc-60* by itself grows poorly.

The *mnT10(V)*-bearing chromosome recombines readily with LGV. Among the hermaphrodite non-Dpy self-progeny of *mnT10(V)/unc-42 unc-51; mnT10(X)/dpy-3* hermaphrodites 34 of 220 were Unc-42 non-Unc-51 recombinants (P = 0.38). Progeny testing of some of these recombinants showed, as expected, that *mnT10(V)* maps much closer to *unc-42* than to *unc-51*; 14 of 15 recombinants gave Dpy (Unc-42) males but no non-Dpy (Unc-42) males.

The proximity of the Him-conferring mutation to the X breakpoint of *mnT10(X)*, indicates that the Him trait is probably due to *mnT10(X)* itself. The two-factor data already cited, as well as the three-factor map data given in Table 1 support this supposition, the Him trait mapping very near or to the left of *dpy-3*. Homozygous *mnT10(X)* animals, which are frequent self-progeny of *mnT10(X)/dpy-3* hermaphrodites, are also Him; they segregated 27% males among 885 self-progeny. The *mnT10(X)* homozygotes comprise two classes; one heterozygous for *mnT10(V)* and one homozygous for *mnT10(V)*; both are Him, but all of the males produced by the latter, genotype *mnT10(V)/mnT10(V); mnT10(X)/0*, are slow developing and sterile. We have confirmed the *mnT10(V)/mnT10(V); mnT10(X)/mnT10(X)* genotype by mating with *lon-2* males; all (28 of 28) cross-progeny hermaphrodites were *mnT10(V)/+; mnT10(X)/lon-2*, giving both Lon male and wild-type male self-progeny.

We note that *mnT10(X)* shows about sevenfold reduced recombination with a normal X in the *dpy-3* to *unc-6* interval: 25 recombinants were found among 791 self-progeny of *mnT10(X)/dpy-3 unc-6* (P = 0.02, where in the calculation of P it has been assumed that a recessive lethal is located to the left of *dpy-3*), compared with 117 recombinants among 758 self-progeny of *dpy-3 unc-6/+ +* (P = 0.17). Recombination in the *dpy-7* to *unc-3* interval was little affected: 111 recombinants were found among 620 self-progeny of *mnT10(X)/dpy-7 unc-3* (P = 0.15), compared with 148 recombinants among 878 self-progeny of *dpy-7 unc-3/+ +* (P = 0.19).

Finally, the production of both nullo-X and diplo-X ova by *mnT10(V;X)* heterozygotes was demonstrated by mating individual *unc-32 III; mnT10(V)/-+; mnT10(X)/dpy-3* hermaphrodites with *lon-2* X males. Nullo-X ova led to the production of Lon males (14% of the 988 cross-progeny scored). Diplo-X ova generated 21 of 136 wild-type hermaphrodite progeny (which were 54% of the cross-progeny), as shown by progeny testing; the diplo-X ova were all *mnT10(X)/dpy-3* and were, therefore, formed by reductional nondisjunction.

mnT7(IV;X), mnT8(V;X) *and* mnT9(I;X): Three additional dominant X-nondisjunction mutants, each of which gave 33–37% male self-progeny (based on

more than 1500 progeny scored for each mutant), proved to carry X-autosome translocations. In all three cases the Him-conferring mutation mapped near *unc-3* X (Table 1), which showed pseudolinkage to *dpy-4 IV* in the case of *mnT7(IV;X)* (one Unc-3 non-Dpy recombinant among 145 hermaphrodite progeny), *unc-60 V* in the case of *mnT8(V;X)* (no Unc-3 non-Unc-60 recombinants among 349 hermaphrodite progeny), and *unc-59 I* in the case of *mnT9(I;X)* (11 Unc-59 non-Unc-3 recombinants among 384 hermaphrodite progeny). In addition, *mnT9* failed to complement *unc-54 I*; a deficiency of the *unc-54* region could help account for the relatively poor growth of the *mnT9*-bearing animals. Linkage of *unc-3* to *dpy-5 I*, *dpy-10 II*, *dpy-18 III*, *dpy-13 IV* and *dpy-11 V* was tested in heterozygotes for each translocation, and no evidence for pseudolinkage other than to the appropriate linkage groups was found. For none of the three translocations were viable homozygous translocation animals found (although X hemizygous males were viable and fertile). Finally, all three of the translocations recombined readily with a normal X homologue; measured recombination frequencies for the *dpy-7* to *unc-3* interval, which is normally about 17% (BRENNER 1974), were 9, 8 and 20%, based on frequencies of hermaphrodite recombinant phenotypes of 24 of 291, 16 of 220 and 38 of 213, for *mnT7*, *mnT8* and *mnT9*, respectively.

DISCUSSION

Seven of the eight dominant X-nondisjunction mutants described in this paper are X-autosome translocations. The eighth mutation, *mn164*, is X linked and shows no pseudolinkage to autosomal markers. Since homozygous *mn164* animals (in addition to heterozygotes) show high-frequency X-chromosome nondisjunction, the nondisjunction is obviously not caused by pairing difficulties due to heterozygosity for a chromosome aberration. Indeed, because of the near-normal recombination between the *mn164*-bearing chromosome and its homologue, it seems likely that synapsis, or at least the initiation of synapsis, of the *mn164*-bearing chromosome in heterozygous hermaphrodites is normal. We suggest that *mn164*, which was identified after X-ray treatment, may involve a structural abnormality of the X chromosome that affects chromosome segregation *per se*. The finding that an *mn164* heterozygote shows equational nondisjunction of the *mn164* mutation but not its wild-type allele supports this view; that is, *mn164* promotes equational nondisjunction in a *cis*-dominant fashion.

It now seems clear that the chromosomes of *C. elegans* are holocentric. We use the term holocentric to cover the general case of a nonlocalized centromere, whether it involves the diffuse attachment of spindle microtubules along a long region of a chromosome or attachment to numerous discrete and localized centromeres of a chromosome (for discussion and references, see JOHN and LEWIS 1965; WHITE 1973; BOSTOCK and SUMNER 1978). No centric constrictions are apparent in stained chromosomes of *C. elegans* prepared for light microscopy, either meiotic (NIGON and BRUN 1955; HERMAN, ALBERTSON and BRENNER 1976) or mitotic (ALBERTSON and THOMSON 1982). Numerous free chromosome duplications have been identified (HERMAN, ALBERTSON and BRENNER 1976;

HERMAN, MADL and KARI 1979; HODGKIN 1980; P. ANDERSON, personal communication; A. ROSE and D. BAILLIE, personal communication). Some free X-chromosome duplications do not overlap in extent certain others (HERMAN, MADL and KARI 1979), implying that the X chromosome does not have a unique centromere. More striking is an autosomal duplication identified by HODGKIN (1980) after acetaldehyde treatment: the chromosome from which the duplication was derived was also recovered; it carries a complementary deficiency, and both the deficiency-bearing chromosome and the free duplication are readily passed on in the same animal during mitosis and meiosis. This finding suggests that the centromere of this chromosome is not localized to either fragment. It also suggests that broken chromosome ends of *C. elegans* may not have to be capped by normal telomeres to be stable; this property has been suggested by work on holocentric chromosomes of other organisms (*e.g.*, see WHITE 1973). More recently and most critical, ALBERTSON and THOMSON (1982) have shown by electron microscopy that the kinetochores and attached spindle microtubules of the mitotic chromosomes of *C. elegans* extend along the entire lengths of the six pairs of chromosomes. Moreover, the meiotic chromosomes, studied in the male, show spindle microtubules inserting themselves directly into the chromosomes in the apparent absence of a kinetochore (D. ALBERTSON, personal communication); this feature is characteristic of certain holocentric chromosomes (for a list of examples, see BOSTOCK and SUMNER 1978).

Holocentric chromosomes have been studied in certain plants, protozoa, insects and nematodes other than *C. elegans,* such as the plant parasitic nematode *Meloidogyne hapla* (GOLDSTEIN and TRIANTAPHYLLOU 1980). Many cytological studies have been conducted on the meiotic behavior of the holocentric chromosomes of insect species belonging to the orders Heteroptera and Homoptera (see WHITE 1973). Chiasmata are generally completely terminalized in these species by diakinesis; thus, any material corresponding to centromeres must be fully divided by this time, with the possible exception of one or both chromosome ends. Some species invariably show one chiasma per bivalent; terminalization then results in a bivalent consisting of two pairs of chromatids connected end-to-end by a terminal chiasma. Indeed, it appears that in several species such bivalents orient equatorially with regard to the spindle at the first metaphase, so that the first anaphase separates synaptic associations. In these cases, the two chromatids of each chromosome usually remain held together end-to-end for the second meiotic division by half of a terminal chiasma, which thus provides the service usually carried out by the centromere of keeping two chromatids together until anaphase II. The chromosomes of *C. elegans* become very small and condensed during late diakinesis, which makes interpretation of their bivalent structure very difficult (indeed, this is a problem with insect holocentric chromosomes as well), but NIGON and BRUN (1955) have interpreted their Feulgen-stained preparations of oogenesis as showing end-to-end associations of homologues at diplotene-diakinesis for all six bivalents. HERMAN, MADL and KARI (1979) identified two X-chromosome duplications, called *mnDp10* and *mnDp25,* that were translocated to the right end of linkage group I and that were recognizable cytologically at a particular stage of diakinesis as

chromosome satellites or terminal knobs. In homozygotes two knobs were observed on opposite ends of a bivalent; only in heterozygotes was a single knob apparent. These observations are consistent with an end-to-end association of LGI homologues. End-to-end associations of homologues have been noted in other nematodes, such as the plant parasitic nematode *Anguina tritica* (TRIANTAPHYLLOU and HIRSCHMANN 1966) and the animal parasite *Strongyloides papillosus* (D. ALBERTSON, personal communication); thus, the pattern discussed here may apply to nematodes generally.

In view of the aforementioned considerations, the position of *mn164* at the left end of the LGX map leads to the suggestion that *mn164* is an aberration that affects chiasma terminalization or end-to-end attachment of X chromosomes occurring near the site of *mn164*. The *cis*-dominant affect of *mn164* on equational nondisjunction can be rationalized fairly easily by such a model. Finally, we note that *mn164* appears to cause no problems during meiosis in XO cells, since males produce equal numbers of nullo-X and haplo-X sperm; the behavior of the single X chromosome during meiosis in the male is also unaffected by the recessive *him* mutations studied by HODGKIN, HORVITZ and BRENNER (1979).

We characterized two of the seven X-autosome translocations in much greater detail than the others: *mnT2(II;X)* and *mnT10(V;X)*. Both appear to be reciprocal translocations; in each case the two constituent half-translocations can be maintained separately in viable animals; and in each case the dominant X chromosome nondisjunction property is conferred by just one of the half-translocations. The ability to separate the half-translocations helped us to assign genetic markers to each half. Figure 2 diagrams the simplest interpretations consistent with all the data for the breakpoints and rejoinings for *mnT2* and *mnT10*.

The two half-translocations comprising *mnT2* are called *mnDp11(II,X;f)* and *mnT11(I;X)*. The phenotypes of animals carrying one or both of these elements are given in Table 6. The element *mnDp11* can exist as a free duplication, being present in addition to the normal chromosome complement, in either hermaphrodites or males; and its meiotic behavior, both in hermaphrodite oogenesis and male spermatogenesis, is similar to that of free duplications studied previously (HERMAN, MADL and KARI 1979). It is worth noting that partial diploidy for the *unc-1* region does not preclude development of fertile males. The half-translocation *mnDp11* is probably smaller than the relative map distance in Figure 2 suggests. Genes tend to map in clusters on the autosomes, one cluster per autosome, and the right end of LGII is a region of low gene density; the region covered by *mnDp11* probably includes less than 15% of the mapped genes on LGII (37 genes total; D. RIDDLE and M. SWANSON, personal communication) and even less of the X chromosome. We have detected cytologically what we take to be *mnDp11* in oocytes of *mnDp11*-bearing hermaphrodites after staining with the fluorescent dye Hoechst 33258. The results (not shown) were virtually identical with those found previously for other free duplications (HERMAN, MADL and KARI 1979); we observed, at diakinesis, a chromosome fragment that was small compared with the chromosomes comprising the six bivalents also present.

TABLE 6

Phenotypes of animals bearing elements of mnT2(II;X) = mnT11(II;X) mnDp11(II, X;f)

Genotype[a]	Phenotype
II/mnT11; mnDp11; X	Him hermaphrodite
II/mnT11; X	Him hermaphrodite, small, reduced fertility
II/II; mnDp11; X/X	Non-Him hermaphrodite
II/mnT11; mnDp11	Fertile male
II/II; mnDp11; X	Fertile male
II/mnT11	Inviable

[a] *II* represents a normal LGII chromosome and X represents a normal X chromosome

In contrast to *mnDp11*, the reciprocal "half" of *mnT2*, called *mnT11*, includes the bulk of both the LGII and X chromosomes and confers the property of X-chromosome nondisjunction. We have shown that *mnT11* disjoins regularly from a normal LGII chromosome and recombines with it. Furthermore, *mnT11* is viable in heterozygous form in the absence of *mnDp11;* such animals, which are fertile hermaphrodites, are, therefore, deficiency heterozygotes for the regions of II and X carried by *mnDp11*. The frequency of recombination between *mnT11* and a normal X chromosome is very low, but the rare recombinant chromosomes that are recovered are the predicted reciprocal recombinant types, with the *mnT11* breakpoint mapping near *dpy-3*, as expected. This suggests that homologous pairing between *mnT11* and X may be infrequent. Heterozygosity for a translocation breakpoint often suppresses crossing over in Drosophila. The degree of suppression depends on the location of the breakpoint, and it has been proposed that particular regions play critical roles in homologous pairing (for review, see ROBERTS 1976; HAWLEY 1980). Certain translocation heterozygotes of *C. elegans* also show reduced recombination, in regions that can extend considerable distances from the breakpoints (HERMAN, ALBERTSON and BRENNER 1976; HERMAN 1978; ROSENBLUTH and BAILLIE 1981; P. DEAK and A. FODOR, personal communication; C. FERGUSON and R. HORVITZ, personal communication). Moreover, ROSENBLUTH and BAILLIE (1981) showed that crossing over in the right half of LGIII, which is suppressed in *eT1(III;V)* heterozygotes, is not suppressed in *eT1* homozygotes, thus showing that heterozygosity for the breakpoint is necessary for the crossover suppression to occur. Heterozygosity for *mnT2* suppresses crossing over along virtually the full extent of the X chromosome. The extent of crossover suppression for different translocation breakpoints is quite variable, and the reason for this is not known. Apart from the position of the X breakpoint, in the case of *mnT11* the apparently very effective pairing with a normal *II* may be relevant. It is curious that two other independently derived dominant X-chromosome nondisjunction mutants, *mnT3* and *mnT6*, appear to be very similar to *mnT2*. The crossover suppressing properties of these translocations may be useful in balancing X-linked lethal and sterile mutations.

Infrequent homologous pairing between *mnT11* and X seems to provide a simple explanation for the high-frequency X-chromosome nondisjunction in *mnT11* heterozygotes. Two additional points must be considered, however.

First, in Drosophila females, for example, a backup system of distributive pairing is available when homologous pairing fails (for review, see GRELL 1976). Distributive pairing must be taken into account when interpreting the effects of heterozygosity for certain X-autosome translocations on X-chromosome nondisjunction in Drosophila (CHANDLEY 1965). It is not clear that distributive pairing occurs in *C. elegans;* several free duplications, such as *mnDp11,* show a tendency to disjoin from the single X in male meiosis (HERMAN, MADL and KARI 1979), but the effect is weak. Distributive pairing does not appear to be a common process, and homologous pairing and exchange appear to be necessary for normal disjunction in most organisms (BAKER *et al.* 1976). The second and more important point is that heterozygosity for some of the other X-autosome translocations that we have studied does not greatly affect X-chromosome recombination but does give high-frequency X nondisjunction; the causes of high nondisjunction to be suggested below both for *mnT10* and for *mnT7, mnT8* and *mnT9* can as well apply to *mnT11,* so poor pairing may not be the sole cause of nondisjunction in *mnT11* heterozygotes.

The two half-translocations comprising *mnT10(V;X)* are called *mnT10(V)* and *mnT10(X)* (see Figure 2). The phenotypes of animals carrying one or both of these elements are given in Table 7. Either element can exist in heterozygous form in the absence of the other; such animals are heterozygous for both a duplication and a deficiency. We have shown that *mnT10(V)* recombines with a normal *V* and that *mnT10(X)* recombines with a normal X; we have no evidence for recombination between *mnT10(V)* and X or between *mnT10(X)* and *V.* The region of LGV carried by *mnT10(X)* includes about 20% of the 44 genes that have been mapped on LGV (D. RIDDLE and M. SWANSON, personal communication).

The Him property conferred by *mnT10(V;X)* is due solely to *mnT10(X),* which carries all of the X chromosome but the left tip. In *mnT10(X)* heterozygotes there is some suppression of crossing over near the left end of the X, but X recombination overall does not seem sufficiently reduced to implicate pairing difficulties as the cause of the high-frequency nondisjunction. Indeed, the fact that *mnT10* homozygotes are also Him indicates that complete chromosome homology does not prevent nondisjunction. We suggest that *mnT10(X)* is defective in disjunction because of the absence of the left tip of the X, which, as we suggested in our discussion of *mn164,* may play an important role in X chromosome segregation, perhaps in maintaining end-to-end association of homologues until anaphase I and chromatids until anaphase II. A prediction of this view, as yet untested, is that deficiencies of the left tip of the X chromosome would lead to nondisjunction. Deficiencies of *unc-3* that seem to extend through the right tip of the X are available (MENEELY and HERMAN 1981). An animal carrying one of these, *mnDf1,* and a normal X chromosome is non-Him (unpublished).

The final set of three X-autosome translocations show striking similarities, although each translocation involves a different autosome. The X breakpoints all map near *unc-3,* which is near the right end of X. The autosomal breakpoints are near the right end of *IV,* the left end of *V* and the right end of *I* for *mnT7,*

TABLE 7

Phenotypes of animals bearing elements of mnT10(V;X) = mnT10(V) mnT10(X)

Genotype[a]	Phenotype
mnT10(V)/V; mnT10(X)/X	Him hermaphrodite
V/V; mnT10(X)/X	Him hermaphrodite
mnT10(V)/V; X/X	Non-Him hermaphrodite sickly, reduced fertility
mnT10(V)/V; mnT10(X)/mnT10(X)	Him hermaphrodite
mnT10(V)/mnT10(V); mnT10(X)/mnT10(X)	Him hermaphrodite
mnT10(V)/V; mnT10(X)/0	Fertile male
mnT10(V)/V; X/*0*	Sickly male
mnT10(V)/mnT10(V); mnT10(X)/0	Sterile male
V/V; mnT10(X)/0	Inviable

[a] V represents a normal LGV chromosome and X represents a normal X chromosome.

mnT8 and *mnT9*, respectively. Translocation heterozygosity in each case leads to a frequency of male self-progeny of about 35%. This very high value may correspond approximately to that expected for no normal X disjunction. It is about what *mnT2* heterozygotes give, and it is the maximum found for recessive *him* mutants, *viz.*, the case of *him-8*, which showed severely reduced X-chromosome recombination (HODGKIN, HORVITZ and BRENNER 1979). The three X-autosome translocations considered here do not show severely reduced X recombination, so we cannot attribute their high nondisjunction frequencies to poor synapsis. Although we do not know how the breakpoints of these translocations are rejoined, we speculate that in each case the bulk of the X is joined to the bulk of the autosome (rather than there being an exchange of chromosomal ends) to produce chromosomes analogous to *mnT11(II;X)* and that the resulting almost double chromosomes disjoin from the normal autosomes rather than the normal X. A prediction of this view would be that homozygous translocations of this class would not be Him; unfortunately, none of these three translocations is homozygous viable.

As more chromosome rearrangements of *C. elegans* are studied, we must look for principles governing their formation and behavior. It seems likely that the principles governing holocentric chromosome rearrangements, about which little is known, may differ from those that obtain for monocentric chromosomes, and that the differences may shed light on the nature of chromosomal evolution.

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