The Effects of Translocations on Recombination Frequency in Caenorhabditis elegans

Kim S. McKim, Ann Marie Howell and Ann M. Rose

Department of Medical Genetics, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5

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ABSTRACT

In the nematode Caenorhabditis elegans, recombination suppression in translocation heterozygotes is severe and extensive. We have examined the meiotic properties of two translocations involving chromosome I, szT1(I;X) and hT1(I;V). No recombination was observed in either of these translocation heterozygotes along the left (let-362- unc-13) 17 map units of chromosome I. Using half-translocations as free duplications, we mapped the breakpoints of szT1 and hT1. The boundaries of crossover suppression coincided with the physical breakpoints. We propose that DNA sequences at the right end of chromosome I facilitate pairing and recombination. We use the data from translocations of other chromosomes to map the location of pairing sites on four other chromosomes. hT1 and szT1 differed markedly in their effect on recombination adjacent to the crossover suppressed region. hT1 had no effect on recombination in the adjacent interval. In contrast, the 0.8 map unit interval immediately adjacent to the szT1(I;X) breakpoint on chromosome I increased to 2.5 map units in translocation heterozygotes. This increase occurs in a chromosomal interval which can be expanded by treatment with radiation. These results are consistent with the suggestion that the szT1(I) breakpoint is in a region of DNA in which meiotic recombination is suppressed relative to the genomic average. We propose that DNA sequences disrupted by the szT1 translocation are responsible for determining the frequency of meiotic recombination in the vicinity of the breakpoint.
and Hartman (1982) study of mnT2(I;X) and mnT10(V;X), suppression around the X-chromosome breakpoint and some enhancement adjacent to the chromosome V breakpoint of mnT10(V) was reported.

In this paper, the meiotic properties of two translocations, szT1(I;X) (Fodor and Deak 1985) and hT1(I;V), are described. For both these translocations the boundary of crossover suppression corresponds to the position of the breakpoint. An unexpected result of our study was the discovery of a threefold increase in recombination frequency that occurred in an interval immediately adjacent to the chromosome I breakpoint of the translocation, szT1.

MATERIALS AND METHODS

C. elegans is a self-fertilizing hermaphrodite (5AA:XX). Males (5AA:OX) are found among the self progeny and result from X chromosome nondisjunction (Hodgkin, Horvitz and Brenner, 1979). They occur at a frequency of approximately 1/700 at 20°C (Rose and Baille 1979a). Wild-type and mutant strains were maintained and mated on Petri plates containing nematode growth medium (NGM) streaked with Escherichia coli OP50 (Brenner 1974). The wild-type strain N2 and some mutant strains of C. elegans var. Bristol were obtained from D. L. Baille, Simon Fraser University, Burnaby, Canada or from the Caenorhabditis Genetics Center at the University of Missouri, Columbia. The following mutant genes and alleles were used (listed by chromosome):

\[
\begin{align*}
I & \quad dpy-5(e61); dpy-14(e188); let-80(g96); let-88(s132); let-362(h86); unc-13(e50); unc-29(e403); unc-54(e190); unc-57(e106); unc-73(e936); unc-74(e883); unc-75(e950); unc-101(m1) \\
II & \quad dpy-10(e128); unc-4(e120) \\
III & \quad dpy-17(e164); dpy-18(e364); sma-2(e502); unc-36(e251) \\
IV & \quad unc-22(s77) \\
V & \quad dpy-11(e224); sma-1(e30); unc-23(e25); unc-42(e270); unc-60(m35) \\
X & \quad dpy-3(e27); dpy-7(sz27); dpy-8(e130); lon-2(e678); unc-1(e179); unc-3(e151); unc-20(e112).
\end{align*}
\]

The map position of these genes is shown in Figures 1 and 2. unc-29(e403) was referred to as an allele of unc-56 in previous publications (Brenner 1974; Rose and Baille 1980); however, these are the same gene (Edgley and Riddle 1987) and the unc-29 designation takes precedence. The following rearrangements were used: szT1(I;X) (Fodor and Deak 1985); eT1(III;V) (Rosenbluth and Baille 1981); dD5(I) (Rose and Baille 1980); nDf24 and nDf25 (Ferguson and Horvitz 1985), sdDp1(Iy) and sdDp2(Iy) (Rose, Baille and Curran 1984). Duplications and deficiencies of chromosome I are shown in Figure 2.

The nomenclature follows the uniform system adopted for C. elegans (Horvitz et al. 1979). When discussing both components of a reciprocal translocation, the formal name (i.e., szT1(I;X), kT1(IV;V)) is used. When discussing the individual component chromosomes of a translocation, the nomenclature describes the structure of the new chromosomes. For example, szT1(I;X) = kX'XszT1 + kX'XszT1 and kT1(IV;V) = kY'YkT1 + kY'YkT1 (as shown in Figure 3). The kX'X terminology implies that the new chromosome carries the right portion of the X chromosome joined to the right portion of chromosome I. The "N" superscript signifies the normal chromosome.

Recombination mapping: Recombination frequencies between pairs of markers were determined by scoring the self progeny of cis-heterozygous hermaphrodites under the conditions described by Rose and Baille (1979a). The recombination frequency, \( p \), was calculated using the formula\[ p = 1 - (1 - R)^n \], where \( R \) is the fraction of marked (non-Wt) recombinant individuals over total progeny (Brenner 1974). Map distances are reported as map units (m.u. = 100\( \phi \)). For standard crosses, the total number of progeny (the denominator) was calculated as \( 4/3 \times (\text{the number of wild type plus one recombinant class}) \). The number of recombinant individuals (the numerator) was calculated as twice the number of the more viable recombinant class (Rose and Baille 1979a).

When the interval being examined is in \( \text{cis} \) to a translocation breakpoint, one of the markers crosses onto the translocation chromosome. When alternate and adjacent-a segregation frequencies are equal (see RESULTS), examination of the Punnett square (Figure 4) for the heterozygote dpy-5 unc-szT1(I;?), where dpy-5 is to the left and unc-szT1 is to the right of the translocation breakpoint, shows that recovery of the Unc recombinant would be expected at a frequency twice that of the reciprocal Dpy recombinant when \( p \) is small. As \( p \) increases, the ratio of Dpy to Unc recombinants will increase.

In these situations, recombination frequency was calculated as:

\[ p = \frac{((4A + 2W) - ((4A + 2W)^2)}{16A(4A + W))^{n/2} (4A + W}) \]

where \( B \) is the number of recombinant Unc progeny and \( W \) is the number of wild types.

When the calculation was based on the number of Dpy progeny, then the recombination frequency was:

\[ p = \frac{((4A + 2W) - ((4A + 2W)^2)}{16A(4A + W))^{n/2} (4A + W}) \]

where \( A \) is the number of recombinant Dpy progeny.

In the unc-101 unc-54 experiments, the translocation breakpoint was to the left of the interval. In this case, the recombination frequency was calculated as:

\[ p = \frac{((4A - 4Ai + 2W + 2Wi)}{((4A - 4Ai + 2W + 2Wi)^2 - 4(4A - 2Ai + 3Ai)^2} \]

where \( A \) is the number of Unc-101 recombinants. The i value is the recombination frequency between the breakpoint and unc-101 (15 m.u., see RESULTS) and was included to compensate for the loss of Wt progeny caused by recombination in this interval. One arrives at Equation 2 if \( i = 0 \) is inserted into Equation 3. Confidence limits of 95% were calculated using the Poisson statistics according to Crow and Gardner (1959).

When the interval examined included a szT1(I;X) breakpoint, aneuploid progeny were observed which had the phenotype of one of the recombinants. When the interval examined spanned a breakpoint, the number of recombinants corresponding to the right marker was modified to compensate for segregation of \( I^X'X\text{szT1} \). The equations below were used to calculate the number of duplication bearing worms in a particular experiment. \( T^* \) is a translocation and the right marker is an unc.

\[ (Wt + Unc) = (T^*) + (T^*)0.03 \text{ or } (Wt + Unc)/1.03 = T^* \]

Dp bearing progeny = (Wt + Unc) - (T^*)

Unc recombinants = scored Unc progeny - Dp progeny.
This equation is based on the scoring of the progeny of dpy-5 unc-13; unc-3/szTI(I;X)(+;lon-2) hermaphrodites described in RESULTS. The ratio of Unc-3 (hyperploid) hermaphrodites to Wt hermaphrodites was 0.03. This compensation only approximates the frequency of aneuploid progeny, however, and does not take into account the varying viabilities observed with different aneuploid-mutant combinations. Therefore, map distance calculated from the recombinant not affected by the aneuploid is more accurate.

**Complementation to duplication strains:** \(1^\times X^{sz}T1\): To map the duplication \(1^\times X^{sz}T1\) with respect to visible mutations, dpy-14; O/szTI(I;X) males were crossed to dpy-5 unc-z hermaphrodites. All the wild-type male progeny were + dpy-14/+dpy-5 + unc-z (because of the \(1^\times X\) pseudolinkage in szTI) and these were mated to dpy-5 dpy-14; \(1^\times X^{sz}T1\) hermaphrodites. With the exception of rare recombinants, wild-type progeny have to carry the \(1^\times X^{sz}T1\) chromosome in addition to the dpy-5 dpy-14 chromosome. From this cross dpy-5 unc-z/dpy-5 dpy-14; \(1^\times X^{sz}T1\) hermaphrodites were isolated (among + dpy-14/dpy-5 dpy-14; \(1^\times X^{sz}T1\) hermaphrodites) and their progeny scored to see if the \(1^\times X^{sz}T1\) chromosome carried unc-z(+). Among the progeny of these hermaphrodites, a large number of Unc-z worms (in the expected ratio of 6 Wt:2 Dpy:1 Dpy Dpy:1 Unc Unc:2 Unc) indicated the \(1^\times X^{sz}T1\) chromosome did not carry unc-z(+). To map \(1^\times X^{sz}T1\) with respect to lethal mutations, unc-13 let-x; unc-3/szTI(I;X) strains were constructed and their progeny observed for the presence of Unc-3 progeny. The
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a) szTl(I;X)

\[
\text{unc-3} \quad \text{unc-20} \quad \text{let-80} \quad \text{unc-29} \quad \text{unc-75} \quad \text{unc-54} \nonumber
\]

\[
\text{t}^{R_X^R} \text{szTl}
\]

\[
\text{unc-1} \quad \text{dpy-3} \quad \text{let-80} \quad \text{unc-13} \quad \text{dpy-5} \nonumber
\]

\[
\text{t}^{L_Y^L} \text{szTl}
\]

\[
\text{unc-60} \quad \text{dpy-11} \quad \text{unc-29} \quad \text{unc-75} \quad \text{unc-54} \nonumber
\]

\[
\text{t}^{R_Y^L} \text{hTl}
\]

\[
\text{let-362} \quad \text{dpy-5} \quad \text{let-80} \quad \text{unc-42} \nonumber
\]

\[
\text{t}^{L_Y^R} \text{hTl}
\]

b) hTl(I;V)

\[
\text{FIGURE 3.—Diagram of the chromosomes comprising szTl(I;X) (a) and hTl(I;V) (b). The orientation of the translocation arms is not known; they are drawn in a manner requiring the least number of breaks. For example, the X\textsuperscript{a} piece of szTl(I;X) could be inverted, but this would require at least two more breaks, one at the tip of the X chromosome and another to cap the unc-20 end.}
\]

\[
\text{FIGURE 4.—Punnett square diagramming the predicted zygotes from a dpy-5 unc-2/hTl(I;V) heterozygote in which recombination occurs between the two recessive markers. The two markers are on the left (dpy) and the right (unc) side of the translocation breakpoint. The first four squares are the nonrecombinant gametes while the second four are the recombinant gametes. The normal chromosome I\textsuperscript{a} is indicated by the markers it carries with abbreviation for dpy-5 (d5) and unc-2 (uz). This diagram can be applied to any translocation of this type.}
\]
presence of the Unc-3s indicated the duplication carried the wild-type allele for the lethal mutation. If found, the Unc-3s were confirmed to be unc-13 let-; unc-3/1\textsuperscript{X}I;unc-T1 by progeny testing.  

\[1\text{V}^\text{h}hT1\]: To map visibles against the duplication, dpy-5 unc-x/+ +; dpy-11 unc-42/+ +; 1\text{V}^\text{h}hT1 strains were constructed and their progeny observed for rescue of the unc-x mutation (i.e., Dpy-5 progeny produced). The dpy-11 unc-42 (V) chromosome was present to monitor the presence of the duplication (1\text{V}^\text{h}hT1 is unc-42(−)). Lethal mutations were mapped in a similar fashion except the strain used was unc-13 let-x/+ +; dpy-11 unc-42/+ +; 1\text{V}^\text{h}hT1.

**New lethal mutations balanced by szTI:** Spontaneous Lon males from the strain AF1, +; dpy-8 + unc-3/ szT1(I;X)[+ +; lon-2 + +], were crossed to dpy-5 unc-13; unc-3 hermaphrodites to construct the strain KR900, dpy-5 unc-13; + unc-3/ szT1(I;X)[+ +; lon-2 + +]. Hermaphrodites from this strain were treated with 1500 rad of γ-radiation (cobalt-60) as recommended by Rosenbluth, Cuddeford and Bailie (1985) and the progeny of individual F1 wild-types were screened for the absence of Dpy-5 Unc-13 Unc-3 offspring. In this way strains carrying lethal mutations induced in the cross-over suppressed regions of either chromosomes I or X were isolated. Strains which failed to produce Unc-3 male progeny after crossing to N2 males were assumed to carry an X-linked lethal mutation and were not analyzed further. Twenty-four lethal bearing strains carrying a lethal mutation on chromosome I were analyzed. The lethals were mapped with respect to the dpy-5 and unc-13 markers (after replacing szTI with a normal chromosome) and tested for complementation with visible and lethal mutations in the region.

**Isolation of hT1(I;V):** The translocation hT1(I;V) was isolated in a screen for mutations which resulted in pseudolinkage between the unlinked markers unc-13(I) and dpy-11(V). unc-23 +/+ unc-42(V) males were treated with 1500 rad γ-radiation and mated to unc-13; dpy-11 hermaphrodites. Wild-type F1 hermaphrodites were plated individually and their progeny were screened for lack of independent assortment of dpy-11 and unc-13. One isolate among 2019 F1 was behaved as a translocation between chromosomes I and V and was named hT1(I;V). No pseudolinkage was detected in hT1 heterozygotes between dpy-5(I) and unc-3(X), unc-4(III), dpy-10(II), unc-22(IV) nor between unc-13(I) and dpy-18(III) (data not shown). The translocation homozygotes are lethal and arrest at mid-larval (L3) stage.

**RESULTS**

The translocation szTI(I;X) was initially isolated by Fodor and Deak (1985) as a dominant chromosome X suppressor of translation. It was induced on a lon-2(e678)(X) chromosome using 7000 R of X-radiation. Their analysis showed that szTI consists of two abnormal chromosomes derived from the normal chromosomes I and X, that the homozygotes arrest as embryos, that heterozygous hermaphrodites produce Lon male self-progeny at a frequency of 0.08–0.12 and recombination was reduced in the dpy-7 – unc-3(X) interval from 19.2 to 0.3 m.u. To characterize this translocation further, we have mapped the physical breakpoints and determined the relationships of these breaks to segregation and recombination in the translocation heterozygote. To summarize the findings of our analysis, szTI(I;X) is composed of two chromosomes, 1\textsuperscript{X}I;szTI and 1\textsuperscript{X}I;szTI. Figure 3a shows the arrangement of these chromosomes. The 1\textsuperscript{X}I;szTI chromosome recombines with and segregates from chromosome I and 1\textsuperscript{X}I;szTI recombines with and presumably segregates from the X chromosome. The experiments leading to these conclusions are described below.

**Characterization of the 1\textsuperscript{X}I;szTI chromosome:**

Hermaphrodites of the genotype dpy-5 unc-13; unc-3/ szT1(I;X)[+ +; lon-2] (strain KR900) segregated Wt hermaphrodites (1009), Lon males (71), Dpy-5 Unc-13 Unc-3s (222 hermaphrodites and 19 males) and Unc-3s (50 hermaphrodites and 17 males). As described below, the genotype of the Unc-3 progeny was found to be dpy-5 unc-13; unc-3; 1\textsuperscript{X}I;szTI (i.e., hyperploid for I\textsuperscript{c} and X\textsuperscript{i}). As one of the translocation chromosomes in szT1(I;X), 1\textsuperscript{X}I;szTI was used to map the translocation breakpoints (see below). In the szT1(I;X) segregation (Figure 5), some of the Unc-3 males could result from normal segregation but the Unc-3 hermaphrodites require a nondisjunction event (e.g., 3:1 segregation). The experiments leading to these results are described below. As shown in Figure 5, the Unc-3 males were expected to equal half the number of wild types. This was not observed probably because of the slow development of these hyperploid males, even when compared to their hyperploid hermaphrodite sisters (data not shown).

Dpy-5 progeny are not recovered from dpy-5; unc-3/ szT1(I;X) hermaphrodites (data not shown). The absence of Dyps (non-Unc-3s) and the low frequency of Unc-3s in these experiments confirmed Fodor and Deak’s (1985) findings that the progeny of szTI heterozygotes show a high degree of pseudolinkage between dpy-5 and unc-3. The presence of a few Unc-3s showed that the pseudolinkage was not 100%. Since the pseudolinkage phenomenon of translocation heterozygotes is the result of both (a) the inviability of aneuploid zygotes and (b) the suppression of recombination between the test genes and their translocation breakpoints, the Unc-3s could have been either viable aneuploid progeny or the result of recombination. The latter was unlikely since crossing-over would have resulted in both Unc-3 and Dpy-5 non-Unc-3 progeny from the dpy-5; unc-3/szT1(I;X) heterozygotes.

Investigation of the presumed aneuploids was done with a strain similar to KR900, but carrying dpy-7 instead of unc-3 (i.e., dpy-5 unc-13; dpy-7/szT1(I;X)[+ +; lon-2]). This strain segregated Dpy-7 progeny. If indeed the Dpy-7 hermaphrodites are dpy-5 unc-13; dpy-7/dpy-7/1\textsuperscript{X}I;szTI, then in crosses to wild-type males, all the F1 wild-type hermaphrodites should be heterozygous for dpy-5 unc-13 and segregate Dpy Uncs in their (F2) progeny; this was in fact observed. Moreover, among the F1 progeny, ½ are expected to
receive \(I^{X}X^{sz}T1\); these should segregate Wts to Dpy Uncs in an 11:1 ratio. The expected segregation for a \(dpy-5\unc-13/+; Dp(I;f)\) is an 11:1 Wt to Dpy Unc ratio (assuming the Dp/Dp worms die). From 25 tested hermaphrodites, 12 were observed to give high Wt:Dpy Unc ratios, and the numbers observed (1853:180) were consistent with an 11:1 ratio. Thus the Dpy-7 (or Unc-3) progeny carry one half of \(szTI(I;X)\), which carries \(dpy-5(+); unc-13(+); \) but no copies of \(dpy-7(+); unc-3(+); \). Since this duplication also adds X chromosome material to the genome, it is possible that X/Dp individuals develop as hermaphrodites. If so, then the above Dpy-7 hermaphrodites could be either \(dpy-5\unc-13/+; +/I^{X}X^{sz}T1\) or \(dpy-5\unc-13/+; dpy-7+/I^{X}X^{sz}T1\). All Dpy-7 hermaphrodites segregated Dpy-7 hermaphrodites, so it is likely that X/Dp worms are male.

The \(I^{X}X^{sz}T1\) duplication chromosome causes X nondisjunction. The Dpy-7 aneuploid hermaphrodites (\(dpy-5\unc-13; dpy-7; I^{X}X^{sz}T1\)) produced Dpy-7 non-Dpy-5 non-Unc-13 males (\(dpy-5\unc-13; dpy-7/0; I^{X}X^{sz}T1\)) as well as hermaphrodites (772 Dpy-7 hermaphrodites, 59 Dpy-7 males and 558 Dpy-5 Dpy-7 Unc-13 hermaphrodites and males). In addition, \(I^{X}X^{sz}T1\) is not recovered in the expected 2:1 Wt/Dpy Unc ratio (831/558 = 1.49). This indicates either decreased viability or meiotic/mitotic loss or both.

Duplication carrying wild-type males in the progeny of \(dpy-5\unc-13; +/szTI(I;X)[+; lon-2]\) hermaphrodites did not mate, a result comparable to that reported by Rose, Baillie and Curran (1984) for \(sDp2(I;f)\) males. The chromosome breakpoint is shown below to map between \(let-88\) and \(let-80\) (Figure 3a).

The chromosome I breakpoint of \(szTI(I;X)\) is shown below to map between \(let-88\) and \(let-80\) (Figure 3a). Strains were constructed with markers on a normal
chromosome I and tested for complementation with wild-type alleles on $I^X{szTl}$ (see MATERIALS AND METHODS). The essential genes $let-88$ and $let-80$ map to the right of $sDf5$ (a deficiency of $unc-13$), but to the left of $unc-29$ (Rose and Bailie 1980) (Figure 2). We have found $let-80$ fails to complement $ndf24$ and $ndf25$ (Figure 2). $I^X{szTl}$ includes the wild type alleles of $let-362$, $dpy-5$, $let-88$ and genes deleted by $sDf5$, but not of $let-80$ or $unc-29$.

Although the translocation homozygotes die, Lon males (e.g., $dpy-5$ $unc-13(O)/szTl(I;X)$) survive. Therefore, the $szTl$-associated lethal mutation does not involve an X chromosome gene (Fodor and Deak 1985). The duplication described by Rose, Bailie and Curran (1984), $sdpl(jf)$, which covers the $unc-74-unc-54$ interval, rescued the $szTl$-associated lethal mutation, placing the lethal mutation to the right of $unc-11$ (Figure 2). The $szTl$-associated lethal mutation is outside both $ndf24$ and $ndf25$. Assuming that the breakpoint generated the lethal site and knowing that $unc-29$ is within $ndf24$ and $ndf25$ (Ferguson and Horvitz 1985) (Figure 2) and to the right of the translocation breakpoint, then the $szTl(I;X)$ breakpoint is to the left of $ndf24$ and $ndf25$.

Segregational properties of $szTl$

$I^X{szTl}$ segregates from chromosome I: An unc-29 marked $I^X{szTl}$ was used to determine which translocation chromosome segregates from the normal chromosome I. $dpy-14$ unc-29; $+/szTl(I;X)[+ unc-29; lon-2]$ hermaphrodites were crossed to $dpy-5$ unc-29; $szTl(I;X)[+; lon-2]$ males. The ratio of $F_1$ wild-type hermaphrodites segregating $Dpy-14$ Unc-29 $F_2$s to those segregating $Dpy-5$ Unc-29 $F_2$s depends on which chromosome $unc-29$ segregates from. If the half-translocation marked with $unc-29a(e103)$ ($I^X{szTl}$) segregates independently of chromosome I in males, sperm containing both $dpy-5$ unc-29 and $I^X{szTl}$ would be produced. If this sperm fertilizes an oocyte containing a normal X and the other half-translocation $I^X{szTl}$, hermaphrodites segregating $Dpy-5$ Unc-29s will be produced. Thirty-two $F_1$ wild-types were tested and all of them segregated $Dpy-14$ unc-29s. We conclude, therefore, that the $I^X{szTl}$ component usually segregates from chromosome I because no $Dpy-5$ Unc-29 segregating $F_1$s were recovered. Since the chromosome I breakpoint lies between $unc-13$ and $unc-29$ and alternate and adjacent-a segregation are equal in hermaphrodites (see below), the other half-translocation, $I^X{szTl}$, must segregate independently of chromosome I in hermaphrodites. As described below, $I^X$ and $I^X{szTl}$ nondisjoin in males, although not as often as expected. Since $I^X{szTl}$ does not carry $dpy-7$ or $unc-3$, these genes must be on $I^X{szTl}$ (see below). $dpy-5$ unc-13; $dpy-7/O; I^X{szTl}$ are not only $Dpy-7$ in phenotype but also male, therefore $I^X{szTl}$ does not carry enough of the X chromosome to produce a hermaphrodite phenotype.

Alternate and adjacent-a are equal in hermaphrodites: The traditional terms alternate-1 and adjacent-2 [see Rickards (1983) for review] cannot be used with C. elegans because the location of a dominant centromere on each chromosome has not been mapped. Therefore, we refer to $I^a$ segregating from $I^N$ (and $I^a$ segregating from $X^N$) as adjacent-a and $I^a$ segregating from $X^N$ (and $I^a$ segregating from $I^N$) as adjacent-b.

$I^X{szTl}$ recombines with the X chromosome (see below), but there is no information concerning its segregation with respect to the normal chromosome I. Several lines of evidence suggest that alternate ($I^X{szTl}$ and $I^X{szTl}$ segregate to the same pole) and adjacent-a ($I^X{szTl}$ and $I^X{szTl}$ segregate to the same pole) occur at equal frequencies during hermaphrodite meiosis. When recombination is scored on chromosome I in a small interval including the $szTl(I;X)$ breakpoint, one recombinant class is expected to be recovered at twice the frequency of its reciprocal if alternate and adjacent-a segregations are equal and no aneuploids survive (see Figure 4 and MATERIALS AND METHODS). 414 recombinants were recovered in the experiments reported in Table 2. This number does not include the $Dpy-5$ Unc-29 and Unc-75 reciprocals because the $Dpy-5$ Unc-29s cannot be scored accurately in a $Dpy-5$ Unc-29 Unc-75 background. The observed ratio of reciprocal recombination progeny ($a/b$) was 176/393 and the expected ratio was 190/379. Clearly the results of these experiments agree with the 2:1 prediction.

The egg survival frequency and progeny ratios also support the proposal that alternate and adjacent-a segregations occur at equal frequency. Figure 5 shows the expected egg survival frequency is between 5/16 (31%) and 9/16 (56%) depending on the survival of aneuploid progeny. Fodor and Deak (1985) observed 31% and we have observed 34% (37 adult hermaphrodites from 110 eggs). In addition, a $dpy-5$ unc-13; unc-3/$szTl(I;X)$ hermaphrodite should segregate wild-type and $Dpy-5$ Unc-13 Unc-3 hermaphrodites in a 4:1 ratio (Figure 4), if there are no 3:1 segregations. We observed 1009:222 or 4.5:1. If adjacent-b segregation also occurs with equal probability, the ratios would be 22% for egg survival and a 6:1 ratio for Wt to $Dpy-5$ Unc-13 Unc-3s. As noted above, there is a low frequency (about 10%) of aberrant 3:1 segregations from X nondisjunction. That is, sperm or oocytes are formed which carry a normal X and the $I^X{szTl}$ chromosome. This inflates the number of wild-type progeny in the above comparison.

Segregation in $szTl(I;X)$ males: To test segregation patterns in the male, $dpy-14$; $szTl(I;X)[+; lon-2]$ males were crossed to $dpy-5$ unc-29; $+/szTl(I;X)[+$.
unc-29; lon-2] hermaphrodites and 40 wild-type hermaphrodite progeny were tested by observing their progeny (F_2). If the I^TX^sT1 chromosome segregates randomly as a univalent with respect to I^TX^sT1 and chromosome I, then F_1 wild types segregating Dpy-5 Unc-29 and Dpy-14 Unc-29 are expected in equal numbers; if it segregates from I^TX^ then only the former are expected. Twenty-seven F_1 hermaphrodites were dpy-14; +/szT1(I;X) (+ unc-29; lon-2) and 13 were dpy-5 unc-29; +/szT1(I;X) (+;lon-2). Assuming alternate and adjacent-a segregations are equal in the hermaphrodite, it appears that I^TX^I^TX^sT1 gamesters are produced twice as often as I^N^T1; O gamesters. We have no explanation for the relative excess of I^N^;I^TX^sT1 gamesters, however, this excess does formally imply that I^TX^sT1 segregates from I^TX^sT1, despite the presumed complete absence of homology. However, this happens only in males, where there is no X homolog. 

1^N^ and X^N^ are linked in szT1(I;X): The I^TX^sT1 chromosome was isolated from szT1(I;X) by creating a segmental aneuploid with sDp2(1); f. dpy-5 unc-29; O/szT1(I;X) males were crossed to dpy-5 unc-29; sDp2 hermaphrodites. Some of the wild-type hermaphrodites (2/15) did not segregate Lon males but did segregate Unc-29 hermaphrodites, indicating sDp2 was present; presumably in the genotype dpy-5 unc-29; I^TX^sT1; sDp2; +/O, and I^N^ carries unc-29(+). To show I^TX^sT1 was present, szT1(I;X) was reconstructed by crossing this strain to dpy-5 unc-13; O/ szT1(I;X) males. Thirteen wild-type progeny were tested (by allowing them to self-fertilize) and eleven were dpy-5 unc-29; +/szT1(I;X). The I^TX^sT1 chromosome in these cases must have come from the maternal parent. The other two wild-types were dpy-5 unc-13; +/szT1(I;X); these got their I^TX^sT1 from the paternal parent. As observed above, the bias in recovering one of the classes of wild-type could be explained by proposing chromosome I and I^TX^sT1 tend to segregate together in the male germ line.

This following experiment shows I^N^ and X^N^ segregate together and are therefore probably linked. Among the progeny of the dpy-5 unc-29/I^TX^sT1; sDp2; +/O hermaphrodites, no wild-type males were observed even though Unc-29 and Dpy-5 Unc-29 males were observed. When I^N^ was present and resulting in a wild-type phenotype, the X^N^ piece was present resulting in a hermaphrodite phenotype.

Spontaneous attachment of I^TX^sT1 and the X chromosome: Two more unusual segregant classes were detected when we examined the progeny of 1104 untreated wild-type hermaphrodites from the strain K900. Thirty-four strains were recovered which failed to segregate Dpy Unc Unc progeny, as if a lethal mutation had been induced in the balanced region of the szT1 heterozygotes. These strains did not, however, behave like a standard szT1 strain. Of the 34 strains, 28 segregated approximately one-third of their progeny as Lon males (class 1) and 6 segregated no Lon males (class 2). This segregation pattern is not characteristic of normal lethal bearing szT1 strains (~10% Lon males). In addition, the class 1 strains often reverted to produce strains similar to the original KR900.

Both class 1 and class 2 strains can be explained with one chromosome structure derived from I^TX^sT1. The new chromosome is hypothesized to carry at least a full complement of X material, for example a fusion I^TX^sT1 and the normal X (X^N^) to produce a I^TX^sT1 chromosome. Class 1 strains would then be dpy-5 unc-13/I^TX^sT1; I^TX^sT1/I^TX^sT1, and the class 2 strains would be dpy-5 unc-13/I^TX^sT1; I^TX^sT1/I^TX^sT1. In the original isolation of these strains, the class 1 strains were isolated more frequently (28:6). This is consistent with the proposal that the class 2 zygotides were derived from nullo-X gametides. Class 2 worms are healthy looking wild types while the class 1 worms are thin and clear, like other strains with a I^N^ duplication. There are, of course, other possible explanations for these results. An expected segregation product from KR900 is dpy-5 unc-13/I^TX^sT1; unc-3/I^TX^sT1/I^TX^sT1. Assuming the I^TX^sT1 chromosomes regularly segregate from each other, this hermaphrodite would have a class 1 phenotype. The derivation of a class 1 strain from a class 2 strain described below, however, does not support this hypothesis.

Analysis of the class 2 strains suggested the normal X chromosome had become physically linked to one of the translocation chromosomes, forming a compound chromosome. When the class 2 strains were crossed to dpy-5/I^N^; +/O males, all Dpy-5 progeny were males. The origin of the X chromosome in these males was shown by crossing the class 2 strains to dpy-7/O males. All the male progeny from this cross were Dpy-7. The abundant patroclinous Dpy-7 males most likely resulted from 100% nondisjunction of the maternal X chromosome centromeres. The failure to recover Dpy-5 hermaphrodites in the initial cross indicated the presumed compound chromosomes segregated away from the normal chromosome I.

The abnormal chromosome in the class 2 strains is the same chromosome which causes the class 1 phenotype. This was shown by crossing unc-11 dpy-14; O/ szT1(I;X) males to a class 2 hermaphrodite strain and observing the F_1 progeny. Twenty-five F_1 progeny were individually set, eight of these segregated the class 1 phenotype and 17 segregated the class 2 phenotype. Thus a class 1-type strain could be derived from a class 2 strain. The failure to recover a strain which segregated Dpy Unc progeny indicated there was no normal X chromosome in the cross. The abnormal chromosome was shown not to be an altered...
form of $I^{RX}$szTI by testing five of the eight class 1 strains for the presence of a $dpy-5$ $unc-13$ chromosome. Since three of the five carried this chromosome, their $I^{RX}$szTI chromosome must have been of paternal origin and not from the original class 1 strain. This test was done by crossing the new class 1 strains to $dpy-5$ $dpy-14/+ +$ males. In these crosses, the class 1 strains segregated rare Dpy males in their progeny, presumably the result of nondisjunction of the two translocation chromosomes containing portions of the X chromosome.

**Chromosome I lethals balanced by szTI**

The KR900 strain was treated with 1500 rad of $\gamma$-radiation and strains which segregated no Dpy Uncs and approximately 10% Lon males were recovered. After crossing to wild-type males, 24 strains behaved as if they carried a lethal mutation linked to $dpy-5$ $unc-13$ (see MATERIALS AND METHODS). Fifteen of these could be mapped; the other nine were more complex. One which mapped to the left of $dpy-5$ has been extensively studied. This mutation is a deficiency, $hDf6$, which deletes $unc-57$, $unc-73$ and $unc-74$.

**Recombination suppression**

Fodor and Deak (1985) observed in szTI(I;X) heterozygotes that recombination is reduced from 19.2 to 0.3 m.u. in the $dpy-7 - unc-3(X)$ intervals. We have found that this suppression includes the $dpy-3 - unc-20$ and $unc-20 - dpy-8$ intervals (Table 1). We also measured recombination in strains that were heterozygous for szTI and chromosome I markers. No recombination was observed from $let-362$ (the left end) to $let-88$ (0.4 m.u. to the right of $unc-13$) (Table 1). Recombination was observed between $unc-13$ and $let-80$, indicating that the boundary of crossover suppression lies between $let-88$ and $let-80$. This boundary appears to coincide with the physical breakpoint of the translocation (Figure 3a).

**Recombination enhancement**

We examined recombination frequencies in chromosome I intervals to the right of the szTI(I;X) breakpoint. Recombination between $unc-13$ and $unc-29$ in szTI heterozygotes was enhanced from 1.2 m.u. to 2.5 m.u. (Table 2). Since no recombination was observed in the $unc-13$ $let-88$ interval (Table 1), all of the increase must have occurred between $let-88$ and $unc-29$. Normal recombination in this interval is less than 0.8 m.u. (1.2 m.u. minus 0.4 m.u.; Table 2, line 2, Table 1, line 11). By the same reasoning, all recombination between $dpy-5$ and $unc-29$ in the szTI heterozygotes (Table 2, lines 2–5 and lines 8–11) must have taken place between $let-88$ and $unc-29$. In the 3 different strains tested, the same level of about 2.5 m.u. was measured. Thus this interval, immediately adjacent to the szTI breakpoint on chromosome I, increased in size threefold in szTI heterozygotes (from <0.8 to 2.5 m.u.). This map expansion extended into the $unc-29$ $unc-75$ interval which increased two-fold from 5.8 to 12.9 m.u. (Table 2). The adjacent interval, $unc-101$ $unc-54$ (Table 2), increased less than twofold in szTI heterozygotes from 14.2 to 24.4 m.u. As described in MATERIALS AND METHODS, this calculation is based in part on the $dpy-5$ $unc-101$ distance in szTI(I;X) heterozygotes (Table 2).

In order to determine if the szTI-enhanced region is one that can be expanded by radiation, we treated $dpy-5$ $unc-13$ $unc-29/+ +$ + + hermaphrodites with 2000 rad of $\gamma$-radiation. In our experiments, the $dpy-5$ $unc-13$ interval increased from 1.9 to 3.3 m.u., an increase comparable to that reported by Kim and Rose (1987) (1.6 to 3.9 m.u.). The $unc-13$ $unc-29$ interval which
spans the position of the szT1 breakpoint increased almost twofold from 1.2 to 2.2 m.u. (Table 2).

On the X chromosome a 50% increase was observed in the unc-1 – dpy-7 interval from 19.7 to 26.3 m.u. (Table 2). The increase is actually larger than 50%, however, because the crossover suppression boundary is near unc-20. unc-20 is approximately 5 m.u. from unc-1 (EDGELY and RIDDLE 1987). Recombination immediately adjacent to the szT1 breakpoint on the X chromosome was not increased compared to our controls. We observed an apparent decrease from 5.0 to 3.0 m.u. in the dpy-3 unc-20 interval in szT1(I;X) heterozygotes (Table 1). Unfortunately, the location of the breakpoint and crossover suppression boundary in the dpy-3 unc-20 interval is not known to the same resolution as on chromosome I.

Enhancement of recombination was restricted to the region to the right of the chromosome I breakpoint. We found no significant enhancement of recombination in several other regions of the genome tested (Table 3), including the dpy-10 unc-4 interval, previously reported by FODOR and DEAK (1985) to increase twofold.

**Comparison of hT1(I;V) to szT1(I;X)**

The isolation of hT1(I;V) is described in materials and methods. It was isolated as a mutation that caused pseudolinkage between unc-13(I) and dpy-11(V). The experiments below describe how we deduced the structure of hT1(I;V). The conclusions are that hT1(I;V) is composed of two chromosomes Irvl—hT1 and Ilvl—hT1 (Figure 3b). Irvl—hT1 segregates from and recombines with chromosome I while Ilvl—hT1 segregates from and recombines with chromosome V.

**Structure of lrvl—hT1:** The half-translocation lrvl—hT1 has been isolated in a free duplication (hyperploid) strain from rare nondisjunction events in the progeny of unc-13; dpy-11/hT1(I;V). The duplication

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**TABLE 2**

Recombination enhancement in szT1(I;X) heterozygotes

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Wts</th>
<th>Recombinants (px100)</th>
<th>p×100 (C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>dpy-5 unc-13 unc-29/+ + +</td>
<td>2678</td>
<td>34 Dpy-5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.9 (1.5–2.6)</td>
</tr>
<tr>
<td>dpy-5 unc-13 unc-29;+/szT1</td>
<td>680</td>
<td>17 Unc-29&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.2 (0.8–2.6)</td>
</tr>
<tr>
<td>dpy-5 unc-29;+/szT1</td>
<td>707</td>
<td>9 Dpy-5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.5 (1.5–3.8)</td>
</tr>
<tr>
<td>dpy-5 unc-29 unc-75;+/szT1</td>
<td>1767</td>
<td>14 Unc-29&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.5 (1.1–4.7)</td>
</tr>
<tr>
<td>dpy-5 unc-29 unc-75;+/szT1</td>
<td>1769</td>
<td>26 Dpy-5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.6 (1.7–3.7)</td>
</tr>
<tr>
<td>dpy-5 unc-13 unc-29/+/ + +</td>
<td>2678</td>
<td>38 Unc-29 Unc-75&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.1 (2.1–4.1)</td>
</tr>
<tr>
<td>dpy-5 unc-13 unc-29;+/szT1</td>
<td>680</td>
<td>70 Unc-75&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5.8 (4.5–7.2)</td>
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<tr>
<td>dpy-5 unc-29 unc-75;+/szT1</td>
<td>1767</td>
<td>26 Dpy-5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.6 (1.7–3.7)</td>
</tr>
<tr>
<td>dpy-5 unc-29 unc-75;+/szT1</td>
<td>1769</td>
<td>66 Unc-29 Unc-75&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12.9 (11.2–14.6)</td>
</tr>
</tbody>
</table>

---

**TABLE 3**

Recombination on other chromosomes

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Wts</th>
<th>Recombinants (px100)</th>
<th>p×100 (C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>dpy-10 unc-4/+/ + (II)</td>
<td>2484</td>
<td>47 Unc-4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.8 (2.1–3.7)</td>
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<tr>
<td>dpy-10 unc-4/+/ +;+/szT1</td>
<td>1163</td>
<td>25 Unc-4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.2 (2.2–4.5)</td>
</tr>
<tr>
<td>unc-36 sma-2/+/ + (III)</td>
<td>1693</td>
<td>4 Unc-36&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.4 (0.09–0.9)</td>
</tr>
<tr>
<td>unc-36 sma-2/+/ +;+/szT1</td>
<td>731</td>
<td>1 Unc-36&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.2 (0–1.0)</td>
</tr>
<tr>
<td>unc-42 sma-1/+/ + (V)</td>
<td>1070</td>
<td>8 Unc-42&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.1 (0.4–2.1)</td>
</tr>
<tr>
<td>unc-42 sma-1/+/ +;szT1</td>
<td>695</td>
<td>4 Unc-42&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.9 (0.2–2.2)</td>
</tr>
<tr>
<td>dpy-11 unc-23/+ + (V)</td>
<td>1186</td>
<td>19 Dpy-11&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.4 (1.4–3.6)</td>
</tr>
<tr>
<td>dpy-11 unc-23/+/ +;szT1</td>
<td>659</td>
<td>14 Dpy-11&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.2 (1.8–5.2)</td>
</tr>
</tbody>
</table>

C.I. = 95% confidence interval.

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<sup>a</sup> See materials and methods. C. I. = 95% confidence interval. The intervals assayed were:

<sup>b</sup> dpy-3 unc13;
<sup>c</sup> unc-13 unc-29;
<sup>d</sup> dpy-5 unc29;
<sup>e</sup> unc-29 unc-75.

Calculated from the sum of both recombinants.

<i>2000 rad γ-radiation.</i>
strain has an Unc-13 phenotype and was found to be of the genotype unc-13; dpy-11(+) IRVLhT1. When this strain was crossed to wild-type males, all the F1 progeny segregated Dpy-11 and Unc-13 progeny. Thus, like the $I^XszT1$ strain, the $I^Y$hT1 strain carried a normal diploid complement in addition to the duplicated region of chromosomes I and V. As with szT1, the duplication strain was used to map the chromosome I breakpoint of the translocation (MATERIALS AND METHODS). Because the duplication strains were Dpy-11(+), $I^Y$hT1 must carry dpy-11(+). In addition, $I^Y$hT1 carries unc-60(+).

The chromosome I breakpoint of $hT1(I;V)$ is between $let-80$ and $unc-29$. This places the $hT1(I;V)$ breakpoint to the right of the $szT1(I;X)$ breakpoint. This was demonstrated through complementation analysis (MATERIALS AND METHODS). $I^Y$hT1 was shown to carry wild-type alleles of $unc-29$ and $unc-75$, but not of $let-80$ or $dpy-5$ (Figure 3b). Knowing that $let-80$ is in $ndf24$ and $ndf25$, the $hT1$ breakpoint must be a region split between these two deficiencies. $hT1(I;V)(unc-29;+)$/[+ $ndf24$; +] $hT1(I;V)(unc-29;+)$/[+ $ndf25$; +] strains were constructed and are viable, suggesting the lethal mutation and the chromosome I breakpoint do not coincide.

**Recombination in $hT1(I;V)$ heterozygotes:** Similar to the observations for szT1, the boundary of crossover suppression correlated closely with the physical breakpoint. The translocation $hT1(I;V)$ (MATERIALS AND METHODS) suppresses recombination in the intervals between $unc-60$ and $dpy-11(V)$ and $let-362$ and $unc-13(I)$ (data not shown). In addition, we observed crossover suppression in the $unc-13 - let-80$ interval (Table 4). On chromosome V, recombination suppression ends before $unc-42$ as Unc-42 recombinants were recovered from $unc-13$; $dpy-11+$/$hT1(I;V)(+;+ unc-42)$ hermaphrodites.

The expected distance between $let-80$ and $unc-29$ is 0.4 m.u. (1.2 minus 0.8 m.u.; Table 2, line 2; Table 1, line 13). We observed 0.5 m.u. between the boundary of crossover suppression and $unc-29$ (Table 4). If there was an increase in this interval as was observed with szT1, it would place the $hT1$ breakpoint very close to, and to the left of $unc-29$. Since we have no genetic markers between $let-80$ and $unc-29$, we cannot be certain if the breakpoint is close to $unc-29$ and there is an enhancement in this region, or if the breakpoint is close to $let-80$ and there is no enhancement. Recombination in the adjacent $unc-29 - unc-75$ interval (as inferred from the $dpy-5$ $unc-75$ experiment since the crossover suppression boundary is very close to $unc-29$) did not increase (5.8 and 6.7 m.u., Tables 2 and 4) as it did for szT1. We conclude that the $hT1(I;V)$ chromosome I breakpoint, which falls in the same general region ($unc-13$ to $unc-29$) as the szT1 breakpoint, does not enhance recombination in the adjacent DNA.

In the $unc-101$ $unc-54$ region, recombination was increased almost twofold from 14.2 to 27.0 m.u. (Tables 2 and 4). As with szT1, this calculation is based partly on the $dpy-5$ $unc-101$ distance in $hT1(I;V)$ heterozygotes (see MATERIALS AND METHODS). In contrast to the region adjacent to the breakpoint, this region behaves similarly in $hT1$ and szT1 heterozygotes.

**Segregation in $hT1(I;V)$ heterozygotes:** Segregation of $I^Y$hT1 was assayed in the following cross. $dpy-5$ unc-13;+/ $hT1(I;V)$ males were crossed to $dpy-5$ $unc-29$; $+/hT1(I;V)(+ unc-29;+)$ hermaphrodites. If $I^Y$hT1 segregated independently of chromosome I, the $dpy-5$ $unc-29$ and $I^Y$hT1 $unc-29$ chromosomes could be in the same oocyte. If fertilized by a $V^R$I$hT1$ sperm, an Unc-29 male would result. From this cross, 247 wild-type males were observed but no Unc-29 males. Thus, as with $szT1(I;X)$, it is the portion of the translocation with the right half of chromosome I ($I^Y$hT1) which usually segregates from chromosome I.

Alternate and adjacent-a segregations appear to occur with equal frequency in $hT1(I;V)$ heterozygotes. The same arguments stated for szT1 apply to $hT1$. From 302 eggs scored from $dpy-5$ unc-13; $+/hT1(I;V)$ parents, 76 reached adulthood, or 25.2%. This value is quite low (expected 31%), suggesting either there is a viability problem or an appreciable level of adjacent-b segregation. The adjacent-b possibility is not likely considering segregation experiments just described. The Wt:Dpy Unc ratio from a $dpy-5$ $unc-29$/ $hT1(I;V)$ heterozygote (Table 4) was close to the expected 4:1 (1636/352 = 4.6:1). For recombination experiments of intervals spanning the chromosome I breakpoint, the ratio of reciprocal recombinants was 58 $dpy-5$ to 122 Unc-$\times$ (or 1:2.1).

**Recombination is not enhanced with a $III(V)$ translocation:** In order to investigate recombination frequency adjacent to the breakpoint of another translocation, the $dpy-17$ $unc-36$($III$) interval was tested in $szT1(III;V)$ heterozygotes. The chromosome III breakpoint of $eT1(III;V)$ is close to or in the $unc-36$ locus.
(ROSENBLUTH and BAILLIE 1981) (Figure 1). We observed 2.2 m.u. (1.8–2.7 m.u.) (25 Dpy recombinants; 1996 wild types) in translocation heterozygotes compared to 1.7 m.u. (1.3–2.0) (25 Dpys; 2211 wild types) in dpy-17 unc-36/+ + controls. If there is an increase in this region, it is not comparable to the magnitude of increase observed adjacent to the szT1 breakpoint on chromosome I. Considering this data and the ht1 data, we conclude that increased recombination adjacent to translocation breakpoints is not a general phenomenon in C. elegans.

**DISCUSSION**

Some of the features of chromosome behavior during meiosis can be revealed by studying the effects translocations have on pairing and recombination. This study of translocations in C. elegans has revealed three distinct effects on meiotic recombination. The first is the suppression of crossing over in translocation heterozygotes, an effect well documented by others (HERMAN 1978; ROSENBLUTH and BAILLIE 1981; HERMAN, KARI and HARTMAN 1982; FERGUSON and HORVITZ 1985, ROSENBLUTH, CUDDEFFORD and BAILLIE 1985). The second is an increase in recombination observed in a homologously paired region removed from the breakpoint. This effect is probably ubiquitous to crossover suppressors. The third alteration is the increase in recombination frequency in homologously paired regions adjacent to the szT1 breakpoint.

In translocation heterozygotes, the crossover suppression boundary and the breakpoint coincide: The two translocations studied in this paper, szT1 and ht1, failed to recombine along the i° segment (~17 m.u.). Using one of the half-translocations as a duplication, we have mapped the breakpoints of szT1 and ht1. In both cases, the boundary of crossover suppression coincides closely with the breakpoint of the translocation and recombination suppression is observed along the left half of chromosome I. In the case of szT1, crossover suppression begins in the interval between let-88 and let-80, where the breakpoint occurs, and continues to let-362 at the left end of the chromosome. Similarly, ht1 which has a breakpoint between let-80 and unc-29, also suppresses recombination from this point to the left end of the chromosome. In both these cases, the crossover suppressed region corresponds to the portion of the translocation which segregates independently of the normal chromosome I.

These findings are in agreement with previous studies where the translocation breakpoints were known. In eT1 (ROSENBLUTH and BAILLIE 1981) and mnT2 (HERMAN, KARI and HARTMAN 1982) heterozygotes, crossover suppression begins at or near a breakpoint and continues to one end of the chromosome. Thus, it seems that in C. elegans translocation heterozygotes, recombination is suppressed on only one side of the breakpoint. One exception is mnT10(V;X), which suppresses recombination around its X chromosome breakpoint (dpy-3 – dpy-7) but not in a more distal region (dpy-7 – unc-3) (HERMAN, KARI and HARTMAN 1982).

Failure to pair as the cause of recombination suppression in translocation heterozygotes has been proposed for D. melanogaster (DOBZHANSKY 1931; SANDLER 1953; ROBERTS 1970; reviewed in ROBERTS 1976; HAWLEY 1980), and maize (BURNHAM et al. 1972). In D. melanogaster, crossover suppression is not perpetuated through the length of translocation arms (reviewed in ROBERTS, 1976). In Drosophila and virtually all other organisms, tetravalent structures and abundant recombination have been observed in translocated regions (reviewed in RICKARDS 1983). Thus there is nothing intrinsic about the configuration of a translocation that would prevent pairing for recombination. As originally proposed by ROSENBLUTH and BAILLIE (1981), the observations of translocation behavior in C. elegans are also most easily explained by the failure of the crossover suppressed region of the chromosome to pair. For example, the portion of chromosome V which in eT1(III;V) is recombinationally suppressed segregates from chromosome III (ROSENBLUTH and BAILLIE 1981). The i° portion which is recombinationally suppressed in szT1 heterozygotes segregates independently of chromosome I.

**1° carries the sequences required for pairing and recombination:** The question of crossover suppression in translocation heterozygotes is a question of homolog pairing. What are the chromosomal features that determine homolog pairing and recombination at meiosis? In maize, pairing has been shown to begin at both ends (not the centromeric region) of chromosomes 1 and 5 (BURNHAM et al. 1972). In D. melanogaster, SANDLER (1953) proposed discrete pairing sites and HAWLEY (1980) provided evidence for the existence and location of four of these sites distributed along the X chromosome. In contrast, CRAYMER (1981) observed recombination between two inversion breakpoints separated by 50 polytene bands, implying that pairing sites are very frequent. Two hypotheses to explain homolog pairing resulting in recombination are (1) pairing by DNA sequence identity or (2) pairing initiating at a specific site(s) on a chromosome and spreading from this site to the rest of the homologous sequence.

It is clear in C. elegans that homolog identity is not determined solely by DNA sequence identity. In translocation heterozygotes, two separate sections of the chromosome each share extensive DNA sequence identity with their homologs, yet only one section pairs and recombines. This recombination can occur right up to the translocation breakpoint. Transloca-
tion homozygotes, however, exhibit recombination in the regions where suppression is observed in heterozygotes (ROSENBLUTH and BAILLIE 1981; K. PETERS, unpublished results). Thus in C. elegans, chromosome pairing may initiate in one region of the chromosome, but then synopsis continues on the basis of DNA sequence identity. In this scenario, recombination suppression is the result of a discontinuity in sequence identity at the breakpoint in translocation heterozygotes.

Consistent with our translocation results are the results from two free duplications which have been studied in C. elegans (ROSE, BAILLIE and CURRAN 1984). Only one of these duplications, sDp1, is capable of pairing and recombining with the normal homolog. This duplication includes the unc-54 end of chromosome I, which pairs and recombines with chromosome I in the translocations sT1 and hT1. The duplication which does not recombine, sDp2, is derived from the left (let-362) end of chromosome I. This is the end which is crossover suppressed in both translocation heterozygotes. Although sDp2 (and also I'X'szT1 and I'X'hT1) may pair with its homolog, it lacks the information to pair for recombination. Therefore, with regard to the localization of sequences involved in homolog pairing for recombination, both the duplication and translocation studies are in agreement. The location of chromosome I homolog pairing (resulting in recombination) sequences can be assigned to I’. These sequences could be one site on I’ or a number of interspersed sites. A third translocation involving chromosome I (K. PETERS and K. McKIM, unpublished results) suppresses recombination in heterozygotes from let-362 to at least unc-101; a region covering about two thirds of the genetic map of chromosome I. This localizes the pairing region to the right of unc-101.

Similarly for other chromosomes for which two or more translocations have been studied, one end of the chromosome can be identified as containing the sequences necessary for homolog pairing and recombination. The homolog recognition sites must lie outside the crossover suppressed region. Three translocations of chromosome III which have been studied are suppressed across intervals at the right (dpy-18) end: eT1(III;V) by ROSENBLUTH and BAILLIE (1981); sT1(III;X) by ROSENBLUTH, CUDDEFORD and BAILLIE (1985); hT2(II;III) by K. PETERS (personal communication). Thus the left (dpy-1) end has the sequences necessary for pairing and recombination. For chromosome IV it is the right (unc-22) end which is crossover suppressed in nT1(IV;V) (FERGUSON and HORVITZ 1985) and sT2(IV;V) (ROSENBLUTH, CUDDEFORD and BAILLIE 1985). In addition, the duplication mDp1(IV;I) (ROGALSKl and RIDDLE 1988) recombines with the normal chromosome IV. This duplication includes the left end of chromosome IV, the same end which pairs and recombines in the translocations described above. For chromosome V, it is the left (unc-60) end which is crossover suppressed in eT1(III;V) (ROSENBLUTH and BAILLIE 1981), nT1(IV;V) (FERGUSON and HORVITZ 1985), sT2(IV;V) (ROSENBLUTH, CUDDEFORD and BAILLIE 1985) and hT1(I;V). The right (unc-51) end carries the sequences which initiate pairing. In the case of the X chromosome, the right (unc-3) end is suppressed in sT1(I;X) (FODOR and DEAK 1985) and mnT2(I;X) (HERMAN, KARI and HARTMAN 1982). Studies on sT1 (FODOR and DEAK 1985; this paper) shows the dpy-3 region pairs and recombines with the normal X chromosome while the portion of the chromosome to the right of dpy-3 is translocated to chromosome I and crossover suppressed. HERMAN and KARI (1988) have come to the same conclusion from the study of X duplications which pair and recombine with the normal X chromosome.

The behavior of the translocation heterozygotes can be understood if, in C. elegans, there is pairing information localized to one end of each chromosome. Since C. elegans chromosomes are considerably smaller than those of Drosophila or maize, it is possible that fewer recognition sequences for pairing are required; possibly only one. This is an interesting suggestion considering the physical nature of C. elegans chromosomes as described by cytogenetics (ALBERTSON and THOMSON 1982). C. elegans chromosomes are holokinetid during mitosis and meiosis; the mitotic or meiotic spindle is observed to attach at many sites along the chromosome. The results and conclusions of this paper can be understood assuming that C. elegans behave as if they are meiotically monocentric. We have not needed to invoke any unusual mechanisms to explain the behavior of the chromosomes reported in this paper.

Recombination frequencies are altered in translocation heterozygotes: Once pairing is established in normal chromosomes, recombination can occur; however the frequency of crossing over is nonuniform along the chromosome. This fact has been demonstrated by studies in Drosophila (reviewed in BAKER et al. 1976; SAUER 1984), yeast (LAMBI and ROEDER 1986) and C. elegans (BRENNER 1974; GREENWALD et al. 1987; KIM and ROSE 1987). SAUER (1984) proposed and mapped elements distributed along the X chromosome of Drosophila which specify the regional distribution of meiotic exchanges. The results presented in this paper suggest that the study of translocation heterozygotes in C. elegans may be a useful approach for identifying chromosomal features which determine the frequency of recombination.

We observed a threefold increase in recombination frequency in the interval adjacent to the sT1 break-
point on chromosome I. An interval of approximately 0.8 m.u. was increased to 2.5 m.u. Previously reported increases of recombination in Drosophila translocation heterozygotes (Hawley 1980; Barabanova, Manon and Vatti 1985) were attributed by Barabanova, Manon and Vatti (1985) to the interchromosomal effect. The interchromosomal effect is a phenomenon where chromosome rearrangements (inversions, translocations) on one chromosome increase and sometimes decrease the general cellular levels of recombination, on both the rearranged chromosome(s) and on the other major chromosomes (for review, see Luchessi 1976). The increases are mostly observed in regions of low intrinsic exchange, such as centromeric regions. We have tested three intervals of low intrinsic exchange (i.e. autosomal gene clusters) on other chromosomes and found no change in the recombination frequency. In addition, enhancement of recombination adjacent to the breakpoint has not been found in other C. elegans translocation heterozygotes. Thus the enhancement adjacent to the slT1 breakpoint cannot be attributed to interchromosomal increases. In addition, enhancement of recombination adjacent to the breakpoint has not been found in other C. elegans translocation heterozygotes and is not likely the result of compensatory increases along the same chromosome.

The twofold enhancement of recombination found in a region (unc-101 – unc-54) removed from the breakpoints of both slT1 and hT1 might reflect a more general response of translocation heterozygotes to recombination suppression. In this situation it is reasonable to propose the enhancement is a compensation for the suppression existing elsewhere on the chromosome. The total recombination on F* in both translocation heterozygotes is approximately 40 m.u., compared to 40–45 m.u. in the normal chromosomes. These "compensatory" increases are strictly an intrachromosomal effect in that they occur on the same chromosome as does the suppression.

The recombination enhancement on the X chromosome may also be compensatory. Our results, however, show only 26 m.u. in the recombining portion of the X chromosome. If this is the extent of the "compensation," then the 10% nondisjunction in hermaphrodites is expected from non-crossover bivalents. To the left of unc-1, however, there may be more crossing over.

The fact that some translocation breakpoints may be accompanied by alterations in recombination in adjacent regions has implications for the use of translocations as genetic balancers. Translocation breakpoints cannot be mapped by means of recombination suppression. Recombination frequency measured across an interval spanning the breakpoint may be altered depending upon whether enhancement or depression of recombination has occurred. In addition, the enhanced recombination which accompanies slT1 affects the maintenance of lethal mutations on chromosome I. Mutations in essential genes to the right of the chromosome I breakpoint are not effectively balanced by this translocation.

In summary, at least three types of translocation-induced alterations in the normal recombination patterns have been observed. The first is suppression of recombination on one side of the break point; this is probably the result of the homologous sequences failing to pair. The second alteration is a general enhancement of recombination in the sequences which pair; this may be caused by compensatory changes resulting from recombination suppression elsewhere on the chromosome. The third is the enhancement of recombination adjacent to the breakpoint of the translocation; as this has only been observed in slT1(I;X) heterozygotes, it may result from a change in the regulation of recombination in the region.

The latter enhancement is of particular interest to us. The region of chromosome I affected by the slT1 breakpoint is part of a gene cluster, a region which contains more genes per map unit than other regions of the linkage map (Brenner 1974). These clusters are found on each autosomal linkage group. The appearance of a cluster on the meiotic map results from a relative suppression of recombination in these clusters compared to the genome average (Greenwald et al. 1987; D. L. Bailie, personal communication). Furthermore, recombination frequency across this interval can be increased by radiation (Kim and Rose 1987; this paper). Regions where the meiotic map is expandable by y-radiation are believed to be those in which recombination per base pair is suppressed relative to the genomic average. Regionality of this type was first observed in Drosophila (Muller 1925). A possibility which we favor is that the slT1 breakpoint on chromosome I disrupts regional constraints on recombination frequency and thus causes an enhancement to the right of the breakpoint. This translocation either removes chromosome I sequences responsible for the suppression of meiotic recombination in this region or introduces X chromosome sequences that eliminate the suppression signals. In either case, the translocation breakpoint may provide a tool for the cloning and molecular characterization of sequences responsible for the regional constraints placed on meiotic recombination frequency.

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