Mutant *rec-1* Eliminates the Meiotic Pattern of Crossing Over in *Caenorhabditis elegans*

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Manuscript received April 6, 1995
Accepted for publication September 11, 1995

ABSTRACT

Meiotic crossovers are not randomly distributed along the chromosome. In *Caenorhabditis elegans* the central portions of the autosomes have relatively few crossovers compared to the flanking regions. We have measured the frequency of crossing over for several intervals across chromosome *I* in strains mutant for *rec-1*. The chromosome is ~50 map units in both wild-type and *rec-1* homozygotes, however, the distribution of exchanges is very different in *rec-1*. Map distances expand across the gene cluster and contract near the right end of the chromosome, resulting in a genetic map more consistent with the physical map. Mutations in two other genes, *him-6* and *him-14*, also disrupted the distribution of exchanges. Unlike *rec-1*, individuals homozygous for *him-6* and *him-14* had an overall reduction in the amount of crossing over accompanied by a high frequency of nondisjunction and reduced egg hatching. In *rec-1; him-6* and *rec-1; him-14* homozygotes the frequency of crossing over was characteristic of the Him mutant phenotype, whereas the distribution of the reduced number of exchanges was characteristic of the Rec-1 pattern. It appears that these gene products play a role in establishing the meiotic pattern of exchange events.

MEIOSIS ensures the faithful transmission of genetic information from generation to generation. During a specialized cell division new combinations of alleles are generated for linked genes, and the diploid chromosome number is reduced by half. In many species, this is accomplished by the pairing of homologous chromosomes, followed by exchange of genetic material, and subsequent disjunction into separate cells in preparation for the second meiotic division. Central to the meiotic process is recombination, which consists of both reciprocal (crossing over) and nonreciprocal (conversion) exchange of information between homologous chromosomes. The frequency of meiotic exchange is important at the cellular level for proper chromosome disjunction, at the individual level for the repair of mutational events, and at the population level for the generation of genetic variation. One approach to elucidating the regulation of recombination is the analysis of mutations that identify genes responsible for the frequency of exchange events and their distribution. In *Drosophila melanogaster* recombination-defective phenotypes are accompanied by a disruption in the normal pattern of crossovers, indicating that both the frequency and distribution of exchanges are genetically regulated (BAKER and CARPENTER 1972; CARPENTER and SANDLER 1974; reviewed by CARPENTER 1988). Those species that use crossing over to promote chromosome segregation require the formation of at least one crossover between homologues to ensure their proper disjunction (reviewed by HAWLEY 1988). The relationship between crossing over and disjunction was recognized by the analysis of mutations that reduce the frequency of crossing over and increase the frequency of nondisjunction for homologous chromosomes at meiosis I (reviewed by BAKER *et al.* 1976).

In *Caenorhabditis elegans* the majority of recessive meiotic mutants have been isolated as mutations that increase the nondisjunction frequency of the *X*, resulting in a *him* (*h*igh *i*ncidence of *m*ales) phenotype (HODGKIN *et al.* 1979). Because the nondisjunction of the *X* chromosome results in aneuploid gametes that can be recovered (both *XXX* and *XO* individuals are viable), a large number of meiotic mutations that affect the *X* chromosome have been recovered. Mutations in *him-1*, *him-5*, and *him-8* disrupt the frequency and distribution of exchange along the sex chromosome with no effect on the autosomes (HODGKIN *et al.* 1979; BROVERMAN and MENEELY 1994). Only a few of the *him* mutations analyzed increase the frequency of nondisjunction of all chromosome pairs (HODGKIN *et al.* 1979; KEMPHUES *et al.* 1988). In the case of *him-6*, the nondisjunction frequency of the autosomes as well as of the *X* chromosome is increased, and those nondisjoining chromosomes are nonrecombinant (HODGKIN *et al.* 1979). Mutations in *him-14* are recombination defective in several intervals that have been tested (KEMPHUES *et al.* 1988; K. KEMPHUES, unpublished results). All of these mutations identify defects in the frequency or distribution of crossovers.

The autosomes of *C. elegans* are marked by a centrally

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located region where genes appear to cluster on the meiotic map as a result of reduced frequency of exchange per unit of physical length (BRENNER 1974; GREENWALD *et al.* 1987; KIM and ROSE 1987; PRASAD and BAILLIE 1989; STARR *et al.* 1989; BARNES *et al.* 1995). These medial gene clusters result both from an increased density of genes and a nonrandom distribution of the sites of meiotic exchange, which is reduced relative to the genomic average near the center of the chromosome and increased in the flanking regions. This reduction in crossing over cannot be explained by the presence of alpha heterchromatic tracts of the type observed in the centromeric regions of Drosophila since no such repetitive sequences were found in the DNA sequence of the chromosome *III* gene cluster (WILSON *et al.* 1994). In addition, cytological observations are incompatible with a meiotic centromere being located within the medial cluster (ALBERTSON and THOMSON 1993), thereby eliminating a centromeric effect as the explanation for the reduced recombination frequency. Thus, at present, there is no obvious explanation for the meiotic pattern of exchange events observed in *C. elegans*.

Insight as to how the distribution of crossover events is regulated has been provided by mutation in the *rec-1* gene. Initially this gene was identified by a mutation resulting in dramatic enhancements of recombination across the medial clusters (ROSE and BAILLIE 1979b), including apparent conversion events (RATTRAY and ROSE 1988). The *rec-1* mutant is not radiation sensitive (HARTMAN and HERMAN 1982), suggesting that the function of the gene product is specific to recombination events rather than to general DNA metabolism and repair. In this paper, we show that while the *rec-1* mutant increases crossing over in the gene cluster of chromosome *I*, exchange is reduced in other intervals, thereby disrupting the normal distribution of exchange events. The total frequency of crossing over along chromosome *I* is not different than controls, suggesting that the function of the *rec-1* gene product is exclusive to determining the meiotic pattern of exchange events rather than their frequency. The interaction of *rec-1* with other mutations that alter crossing over was examined in *rec-1; him-6* and *rec-1; him-14* double mutants. Our results implicate the *rec-1* gene product in the establishment of the normal pattern of meiotic exchange along the *C. elegans* autosomes.

MATERIALS AND METHODS

General methods: *C. elegans* populations consist largely of self-fertilizing hermaphrodites (5A;*XX*). Males (5A;*XO*) arise spontaneously in the progeny of hermaphrodites from *X*-chromosome nondisjunction at a frequency of 0.001 at 20° (HODGKIN *et al.* 1979; ROSE and BAILLIE 1979a) and are maintained by crossing to hermaphrodites. All strains were maintained and mated on petri plates containing nematode growth medium (NGM) and streaked with *Escherichia coli* strain OP50 (BRENNER 1974). All experiments were carried out at 20°. The wild-type strain N2 and most of the mutant strains were obtained from D. L. BAILLIE at Simon Fraser University, Burnaby or from the Caenorhabditis Genetics Center at the University of Missouri, Columbia (now located at the University of Minnesota, Minnesota). KK312, carrying the temperature-sensitive allele *it44* of *him-14*, was kindly provided by K. KEMPHUES, Cornell University, Ithaca. The following genetic markers were used: LG *I, bli-3(e579); unc-11(e47); dpy-5(e61); dpy-14(e188); unc-13(e450); unc-101(m1); unc-54(e190); rec-1(s180)* and LG *V, dpy-11(e224); unc-42(e270)*. The map positions of some genes on chromosome *I* are shown in Figures 1 and 2. The following rearrangements were used in this study and their known breakpoints are shown in Figure 2; the free duplications *sDp1(I;f)* and *sDp2(I;f)* (ROSE *et al.* 1984) and the deficiencies *eDf4(I), eDf9(I), eDf10(I)* and *eDf24(I)* (ANDERSON and BRENNER 1984) are shown in Figure 2.

Recombination mapping: Recombination frequency in the hermaphrodite was measured by scoring the number of recombinant progeny of a *cis*-heterozygote under the conditions described by ROSE and BAILLIE (1979a). The recombination frequency (p) between two markers was calculated using the formula $p = 1 - (1 - 2R)^{1/2}$, where R is the number of visible recombinant individuals divided by the number of total progeny (BRENNER 1974). The number of total progeny for the hermaphrodite was calculated as 4/3 X (number of Wts + one recombinant class). Both classes of recombinants were used in the calculations unless otherwise noted. In cases where only one class of recombinants was used, $R = 2X$ (one recombinant class) divided by the total progeny number. In the case of the *bli-3 unc-11* interval, Bli-3 penetrance is low and Bli-3 recombinants were scored as wild type and later subtracted based on the number of Unc-11 recombinants. Confidence intervals (95%) were calculated using the statistics of CROW and GARDNER (1959). In cases where the number of recombinants exceeded 300, confidence intervals were calculated using the equation $1.96(nxy)^{1/2}$, where n is the number of recombinants, x is the number of recombinants divided by the number of wild types plus recombinants, and y is equal to $1 - x$.

Measuring crossing over in *him-6; rec-1* and *him-14; rec-1* double mutants: The frequency of crossing over in *him-6; rec-1* or *him-14; rec-1* homozygotes was determined by mating *him-6; rec-1* or *him-14; rec-1* homozygous males to hermaphrodites of the genotype *dpy-5 unc-13 rec-1; him-6* or *dpy-5 unc-13 rec-1; him-14*, respectively, and the same procedure was followed for the other intervals measured. The resulting wild-type hermaphrodite progeny were individually plated and the frequency of crossing over measured using the general mapping methods described above.

Nondisjunction frequency: The frequency of nondisjunction of the *X* chromosome was measured by individually plating *rec-1, him-6, him-6; rec-1, him-14*, or *him-14; rec-1* L4 homozygous hermaphrodites and scoring the number of males amongst their progeny.

Egg-hatching frequency: *rec-1; him-6* and *rec-1; him-14* homozygous hermaphrodites and *rec-1, him-6* and *him-14* homozygous controls were individually plated and allowed to lay eggs for one 18-hr period. The hermaphrodites were then removed, and the eggs remaining on the plate were counted. All resulting progeny were counted 4–5 days later.

Measuring double-crossing over: The frequency of double-crossing over was measured by mating *dpy-5 unc-101 unc-54 rec-1/+ + + rec-1* and *dpy-5 unc-101 unc-54/+ + +* males to 10–12 *dpy-5 unc-101 rec-1* or *dpy-5 unc-101* homozygous hermaphrodites for 24 hr. The progeny of mated hermaphrodites were screened for the presence of Unc-101 hermaphrodite recombinants and all wild-type hermaphrodite progeny counted. All Unc-101 recombinants were progeny tested to

determine if they were of the genotype + *unc-101/dpy-5 unc-101*, indicating they arose from a double crossover in the male sperm.

Duplication mapping of *rec-1*: The possibility that *sDp1(I;f)* included the *rec-1* locus was examined by measuring recombination in the *dpy-5 dpy-14* interval in the presence of the duplication (*sDp1* carries wild-type alleles of both of these markers). Rec-1 or N2 males were mated to *dpy-5 dpy-14 rec-1/dpy-5 dpy-14 rec-1/sDp1(I;f)* hermaphrodites and *dpy-5 dpy-14/dpy-5 dpy-14/sDp1(I;f)* controls, respectively. Wild-type hermaphrodite progeny resulting from this cross were individually plated and their progeny scored. *sDp1*-bearing hermaphrodites have lower brood sizes (duplication homozygotes are inviable) and increased *X*-chromosome nondisjunction that results in male progeny (ROSE *et al.* 1984). To identify the individuals that carried the duplication, broods of the size characteristic for *sDp1(I;f)* were examined for the presence of males, and the frequency of the double homozygote class was determined. This class was expected to approach a frequency of 0.125 in the presence of the duplication and a frequency of 0.25 in its absence. The frequency of crossing over in individuals lacking the duplication was calculated as described above in the general mapping methods. A gametic frequency of 0.43 for *sDp1(I;f)* (ROSE *et al.* 1984) was used to calculate the frequency of crossing over in individuals determined to be of the genotype *dpy-5 dpy-14 rec-1/ + + rec-1/ sDp1(I;f)* and *dpy-5 dpy-14 +/+ + rec-1/sDp1(I;f)* using the formula:

$$p = 1 - [1 - 148D/17(D + W)]^{1/2},$$

where D is the number of Dpy-5 recombinants and W is the number of wild-type progeny. This formula is based on the assumptions that the *sDp1* homozygote is inviable and that recombination between *sDp1* and LG *I* does not occur in the *dpy-5 dpy-14* interval (ROSE *et al.* 1984; MCKIM *et al.* 1993). Similarly, *sDp2* was used to map *rec-1* by measuring crossing over in *dpy-5 dpy-14 rec-1/+ + rec-1/sDp2(I;f)* hermaphrodites and in *dpy-5 dpy-14 rec-1/+ + +/sDp2* controls. This duplication covers both markers and *sDp2*-bearing worms were identified by the frequency of segregation of the double mutant as described for *sDp1*. A gametic frequency of 0.38 for *sDp2(I;f)* (ROSE *et al.* 1984) was used to calculate the frequency of crossing over in the presence of the duplication using the formula:

$$p = 1 - [1 - 75D/19(D + W)]^{1/2},$$

where D is the number of Dpy-5 progeny and W is the number of wild types. This formula assumes that the *sDp2* homozygote is not viable. Crossing over was also measured in *dpy-5 unc-13 rec-1/+ + rec-1/sDp2* hermaphrodites and in *dpy-5 unc-13 rec-1/+ + +/sDp2* controls. In this case, however, the duplication does not extend to *unc-13* and as a result, *sDp2*-bearing hermaphrodites were identified by the presence of a large number of Unc-13 segregants amongst their progeny. Recombination in the *dpy-5 unc-13* interval was calculated using the formula:

$$\frac{p = 1 - [1 - 19D/(D + W)]^{1/2}}{16},$$

where D is the number of Dpy-5 recombinants and W is the number of wild-type progeny.

Deficiency mapping of *rec-1*: To test if the ribosomal deficiency *eDf24(I;f)* deleted the *rec-1* locus, *dpy-11 unc-42/+ +; rec-1/rec-1* or *dpy-11 unc-42/+ +* males were crossed to *unc-54/ eDf24* hermaphrodites and the resulting wild-type progeny individually plated. Since *eDf24* does not include *unc-54*, only plates that segregated Dpy-11 Unc-42 progeny and failed to segregate Unc-54 individuals (indicating the presence of the deficiency) were scored. Recombination was measured in the *dpy-11 unc-42* interval using the general recombination formula discussed above. The deficiencies *eDf4, eDf9, eDf10,* and *eDf13* were isolated using *eDf24* as a balancer, and all complement *eDf24* and fail to complement *unc-54* (ANDERSON and BRENNER 1984). To test if any of these deficiencies included *rec-1, eDfX/eDf24* hermaphrodites were mated to *unc-54/+* males, and the resulting Unc-54 hermaphrodites were then mated to males of the genotype *dpy-11 unc-42/+ +; rec-1/rec-1* or *dpy-11 unc-42/+ +*. Wild-type hermaphrodite progeny were individually plated, and their progeny were screened for the presence of Dpy-11 Unc-42 segregants and the absence of Unc-54 segregants. The frequency of crossing over in the *dpy-11 unc-42* interval was then measured and calculated as described above for *eDf24*.

RESULTS

The *rec-1* mutation alters the distribution of a normal number of exchanges: ROSE and BAILLIE (1979b) showed that *rec-1* greatly enhanced the frequency of crossing over in small intervals across the autosomal cluster, however, its effect in larger intervals was not known. To determine the effect of *rec-1* on the frequency of exchange along the whole chromosome, four intervals spanning LG *I* were examined and the results are shown in Figure 1 (data shown in Table 1). The most distal markers used were *bli-3*, near the left end of the chromosome, and *unc-54*, near the right end. The *bli-3 unc-11* interval, located on the left arm of LG *I*, did not significantly change from 14.8 m.u. in controls to 12.8 m.u. in *rec-1* homozygotes. In the medial cluster, however, crossing over was enhanced threefold for the *unc-11 dpy-5* (2.3 to 6.7 m.u.) interval and nearly fourfold for the *dpy-5 unc-13* interval (1.6 to 6.3 m.u.). The *dpy-5 unc-101* interval, normally 12.0 m.u., expanded to 21.2 m.u. in *rec-1* homozygotes. Most of this increase appears to be in the *dpy-5 unc-13* portion of this interval, since calculating the *unc-13 unc-101* interval by subtraction, the increase in *rec-1* homozygotes goes from 10.4 to 14.9 m.u.. In sharp contrast, the *unc-101 unc-54* interval, located on the right arm of the chromosome, was severely reduced from 14.4 m.u. in controls to 4.6 m.u. in *rec-1* homozygotes. The entire *dpy-5 unc-54* interval, however, was unchanged (31.6 m.u. in controls and 30.6 m.u. in *rec-1* homozygotes). Thus, the total frequency of exchange on the right arm of LG *I* did not change in the *rec-1* mutant. The genetic length of LG *I* was 45.3 m.u. in *rec-1* homozygotes and 43.5 m.u. in wild-type controls, consistent with the formation of one chiasmata every meiosis.

The *rec-1* mutation eliminates the meiotic cluster: On the standard genetic map the number of kilobase pairs per map unit increases threefold over the genomic average (1×10^5 kb/300 m.u. = 313 kb/m.u.) in the *dpy-5 unc-13* interval (Table 2), demonstrating that the meiotic pattern of crossing over is nonrandom. The increase is eliminated in *rec-1* homozygotes, and the amount of DNA per map unit becomes a flat distribu-

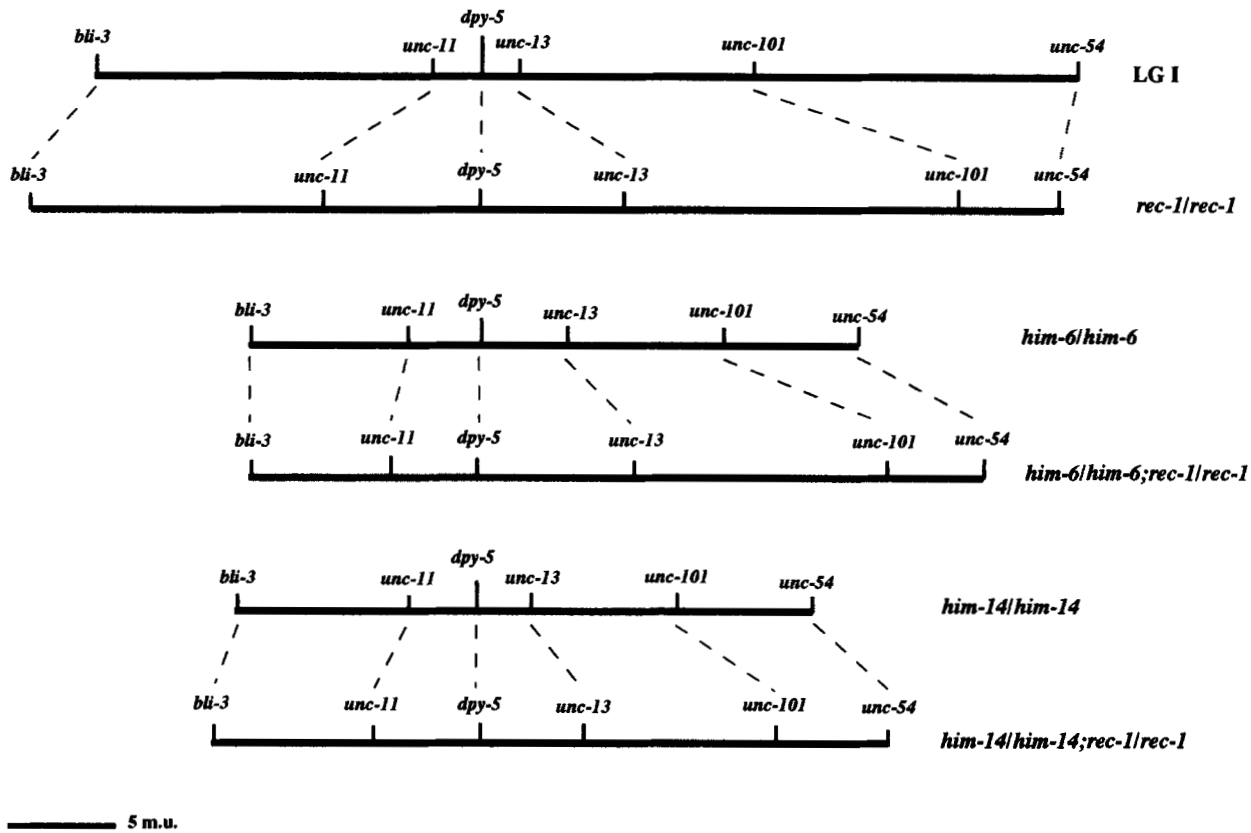

FIGURE 1.—The effects of meiotic mutations on the frequency and distribution of crossing over on chromosome *I*.

tion, which is close to the genomic average for most of the chromosome *I* map. Map distances in the *rec-1* mutant strain approximate the physical distances between markers, with the exception of the *bli-3 unc-11* interval. To calculate the physical distance, physical map positions from BARNES *et. al.* (1995) were used. Physical positions for each of the markers except *bli-3* were available. In the case of *bli-3*, the *sup-34* physical position was used, but since the physical distance between these markers is not known, and as this interval contains many YAC-bridged gaps, the real physical length may be longer, accounting for the result. Alternatively, there may be difference in *rec-1* function in this region, however, *rec-1* homozygotes increase crossing over between *bli-3* and *unc-35* (RATTRAY and ROSE 1988), making this explanation less likely. The result is that *rec-1* mutants produce a map that looks like the physical map.

***him-6* and *him-14* mutations alter the distribution of a reduced number of exchanges:** The initial characterization of *him-6* demonstrated that the nondisjoining chromosomes in homozygotes were also nonrecombinant, implying that mutants were defective in establishing the normal frequency of exchange (HODGKIN *et al.* 1978). Crossing over in four intervals spanning chromosome *I* was measured in *him-6* and *him-14* homozygous individuals (data shown in Table 1). Because nonconditional Him-14 mutants give very few progeny (<5% of the eggs hatch), we used the temperature-sensitive allele *it44* (35% of the eggs hatch at 20°C) (J. DUFFY and K. KEMPHUES, unpublished results). Exchange in the *bli-3 unc-11* interval was reduced from 14.8 m.u. in wild-type controls to 7.1 m.u. in *him-6* mutants and 7.5 m.u. in *him-14* mutants. Crossing over in the *unc-11 dpy-5* interval, however, was enhanced from 2.3 m.u. in controls to 3.1 m.u. in *him-6* homozygotes and 3.5 m.u. in *him-14* homozygotes. The *dpy-5 unc-13* interval showed similar crossover enhancement; the size of the interval increased from 1.6 m.u. in controls to 3.1 m.u. in *him-6* mutants and 2.3 m.u. in *him-14* mutants. Crossing over in the *dpy-5 unc-101* interval was not significantly different between wild-type controls (12.0 m.u.) and *him-6* homozygotes (10.7 m.u.) but was slightly reduced in *him-14* homozygotes (8.8 m.u.). In the *dpy-5 unc-54* interval, however, crossing over was reduced approximately twofold in both mutants: 16.4 m.u. in *him-6* mutants and 14.3 m.u. in *him-14* mutants, compared to 31.6 m.u. in controls. The distribution of crossovers is intermediate between wild type and Rec-1 (Table 2). There is a medial cluster in the Him mutants but not as pronounced as in wild type. The total genetic length of chromosome *I* is nearly half the control value (26.6 m.u. in *him-6* homozygotes and 25.3 in *him-14* homozygotes), indicating that fewer exchanges occur in these mutants.

Crossing over in double mutants has the *rec-1* distribution and the *him* frequency: We investigated the fre-

TABLE 1

Crossing over in meiotic mutants

Genotype	Wild types[a]	Recombinants[b]	pX100(C.I.)[c]
bli-3 unc-11/+ +[d]	1686	170 Unc	14.8 (12.4–17.4)
bli-3 unc-11 rec-1/+ + rec-1	990	79 Unc	12.8 (10.0–16.1)
bli-3 unc-11/+ +; him-6/him-6	1209	55 Unc	7.1 (5.2–9.2)
bli-3 unc-11 rec-1/+ + rec-1; him-6/him-6	2395	96 Unc	6.2 (4.9–7.5)
bli-3 unc-11/+ +; him-14/him-14	847	41 Unc	7.5 (5.2–10.3)
bli-3 unc-11 rec-1/+ + rec-1; him-14/him-14	902	40 Unc	6.9 (4.9–9.4)
unc-11 dpy-5/+ +[d]	3786	58 Dpy	2.3 (2.0–2.8)
unc-11 dpy-5 rec-1/+ + rec-1[d]	2033	91 Dpy 91 Unc	6.7 (5.7–7.6)
unc-11 dpy-5/+ +; him-6/him-6	982	18 Dpy 23 Unc	3.1 (2.2–4.2)
unc-11 dpy-5 rec-1/+ + rec-1; him-6/him-6	1613	41 Dpy 43 Unc	3.9 (3.1–4.8)
unc-11 dpy-5/+ +; him-14/him-14	1298	30 Dpy	3.5 (2.4–4.8)
unc-11 dpy-5 rec-1/+ + rec-1; him-14/him-14	1160	36 Dpy 38 Unc	4.7 (3.8–5.9)
dpy-5 unc-13/+ +[d]	3119	34 Dpy 32 Unc	1.6 (1.2–2.0)
dpy-5 unc-13 rec-1/+ + rec-1	3706	156 Dpy	6.3 (5.3–7.3)
dpy-5 unc-13/+ +; him-6/him-6	2156	46 Dpy 43 Unc	3.1 (2.5–3.8)
dpy-5 unc-13 rec-1/+ + rec-1; him-6/him-6	1922	86 Dpy 88 Unc	6.7 (5.8–7.7)
dpy-5 unc-13/+ +; him-14/him-14	1564	27 Dpy 22 Unc	2.3 (1.7–3.0)
dpy-5 unc-13 rec-1/+ + rec-1; him-14/him-14	1988	84 Dpy 64 Unc	5.5 (4.7–6.4)
dpy-5 unc-101/+ +[e]	889	79 Dpy 66 Unc	12.0 (10.0–14.0)
dpy-5 unc-101 rec-1/+ + rec-1	1369	183 Dpy 213 Unc	21.2 (20.1–22.2)
dpy-5 unc-101/+ +; him-6/him-6	1198	89 Dpy 84 Unc	10.7 (9.1–12.2)
dpy-5 unc-101 rec-1/+ + rec-1; him-6/him-6	961	130 Dpy 105 Unc	17.9 (15.6–20.3)
dpy-5 unc-101/+ +; him-14/him-14	963	67 Dpy 48 Unc	8.8 (7.3–10.6)
dpy-5 unc-101 rec-1/+ + rec-1; him-14/him-14	980	89 Dpy 80 Unc	12.7 (10.9–14.7)
unc-101 unc-54/+ +[d]	1187	116 Unc-101	14.4 (11.8–17.1)
unc-101 unc-54 rec-1/+ + rec-1	1973	61 Unc-101	4.6 (3.6–5.8)
dpy-5 unc-54/+ +	1620	349 Dpy	31.6 (30.3–32.9)
dpy-5 unc-54 rec-1/+ + rec-1	1698	355 Dpy	30.6 (29.2–32.0)
dpy-5 unc-54/+ +; him-6/him-6	1239	138 Dpy	16.4 (13.7–19.3)
dpy-5 unc-54 rec-1/+ + rec-1; him-6/him-6	1807	269 Dpy	21.8 (19.2–24.4)
dpy-5 unc-54/+ +; him-14/him-14	852	83 Dpy	14.3 (11.6–175)
dpy-5 unc-54 rec-1/+ + rec-1; him-14/him-14	805	98 Dpy	17.9 (14.6–21.5)

[a] Male progeny included.
[b] Male recombinants included.
[c] C.I. = 95% confidence interval. See MATERIALS AND METHODS.
[d] Data from ZETKA and ROSE (1990).
[e] Data from ZETKA and ROSE (1992).

TABLE 2

Physical and genetic distances

	bli-3 unc-11	*unc-11 dpy-5*	*dpy-5 unc-13*	*unc-13 unc-101*	*unc-101 unc-54*	Averages
Physical (kb)	1716[a]	1754	2016	5366	1385	12,237
Wild type (m.u.)	14.8	2.3	1.6	10.4	14.4	43.5
kb/m.u.	97	741	1,291	516	96	281
rec-1 (m.u.)	12.8	6.7	6.3	14.9	4.6	45.3
kb/m.u.	134	254	328	300	301	270
him-6 (m.u.)	7.1	3.1	3.1	7.6	5.7	26.6
kb/m.u.	242	550	666	706	243	460
him-14 (m.u.)	7.5	3.5	2.3	6.5	5.5	25.3
kb/m.u.	229	487	898	825	252	484
him-6; rec-1 (m.u.)	6.2	3.9	6.7	11.2	3.9	31.9
kb/m.u.	277	437	308	479	355	384
him-14; rec-1 (m.u.)	6.9	4.7	5.5	7.2	5.2	29.5
kb/m.u.	249	363	375	745	266	415

Physical distances were taken from BARNES *et al.* (1995) and genetic frequencies from Table 1.
[a] kb between *sup-34* and *unc-11*.

TABLE 3

X-chromosome nondisjunction and egg-hatching frequencies in meiotic mutants

Genotype	Male[a]/total progeny	Frequency	Hatched eggs/ total eggs	Frequency
rec-1/rec-1	3/2211	0.001	393/403	0.975
him-6/him-6	178/1416	0.111	20/674	0.029
him-6/him-6; rec-1/rec-1	198/1282	0.133	93/420	0.221
him-14/him-14	243/883	0.215	186/614	0.302
him-14/him-14; rec-1/rec-1	333/1189	0.218	304/965	0.315

[a] Males in the progeny of hermaphrodites were scored as in indicator of *X*-chromosome nondisjunction.

quency and pattern of meiotic exchange on chromosome *I* in *him-6; rec-1* and *him-14; rec-1* double mutants (results shown in Figure 1, data shown in Tables 1 and 2). In the *bli-3 unc-11* interval, the number of exchanges did not significantly differ for the Him strains, *him-6; rec-1* (6.2 m.u.), *him-14; rec-1* (6.9 m.u.), *him-6* (7.1 m.u.), or *him-14* (7.5 m.u.) but was lower than in *rec-1* homozygotes (12.8 m.u.). In the *dpy-5 unc-11* interval, exchange was slightly enhanced from 3.1 m.u. in *him-6* homozygotes to 3.9 m.u. in the double mutant and from 3.5 m.u. in *him-14* homozygotes to 4.7 m.u. in the double mutant. The *dpy-5 unc-13* interval was enhanced twofold in both *him-6; rec-1* (6.7 m.u.) and *him-14; rec-1* (5.5 m.u.) compared to single mutant controls (3.1 m.u. in *him-6* and 2.3 m.u. in *him-14* homozygotes). Crossing over in the *dpy-5 unc-101* interval was enhanced from 10.7 m.u. in *him-6* homozygotes to 17.9 m.u. in the double mutant and from 8.8 m.u. in *him-14* homozygotes to 12.7 m.u. in the double mutant. The total level of exchange between *dpy-5* and *unc-54* was 16.4 in *him-6* homozygotes, compared to 21.8 in the double mutant and 14.3 in *him-14* homozygotes, compared to 17.9 in the double mutant. The total genetic length of chromosome *I* in *him-6; rec-1* homozygotes was 31.9 m.u. (compared to 26.6 in *him-6*) and 29.5 m.u. in *him-14; rec-1* homozygotes (compared to 25.3 m.u. in *him-14*). The total number of crossovers remains at a level characteristic for *him-6* and *him-14,* however, the distribution of exchanges in the double mutants is generally similar to the Rec-1 pattern. The exception is the *unc-13 unc-101* interval in the *him-14; rec-1* double mutant.

***rec-1* mutants have normal frequencies of egg hatching:** *him-6* and *him-14* were originally identified by mutations resulting in a high incidence of males accompanied by a low frequency of egg hatching due to increased nondisjunction of all chromosomes (HODGKIN *et al.* 1978; KEMPHUES *et al.* 1988, respectively). We examined these phenotypes in *rec-1* homozygotes. In contrast to the Him's, Rec-1 mutants have a low frequency of *X*-chromosome nondisjunction (0.001) and a high frequency of egg-hatching (0.975; data shown in Table 3). The frequency of *X*-chromosome nondisjunction we observed in *him-6* was 0.111 and in *him-14* homozygotes 0.215, accompanied by low frequencies of egg hatching (0.029 and 0.302; Table 3). These data, together with the finding that the total number of crossovers is unchanged, support the conclusion that the *rec-1* mutation does not cause increased nondisjunction resulting in egg inviability.

***rec-1* mutants do not increase the frequency of double-crossing over:** We examined the frequency of recovering two crossovers from a single bivalent. The effect of *rec-1* on the frequency of double-crossing over was measured in the male, because double crossovers have not been detected in hermaphrodites (HODGKIN *et al.* 1979; HOWELL *et al.* 1987; K. MCKIM and M. ZETKA, unpublished results). Crosses mating *dpy-5 unc-101 rec-1* hermaphrodites with *dpy-5 unc-101 unc-54 rec-1/+ + + rec-1* males and using *dpy-5 unc-101* hermaphrodites with *dpy-5 unc-101 unc-54/+ + +* control males were done. In the *rec-1* experiment, four Unc-101 hermaphrodites (that did not segregate any Unc-54 progeny) were observed in ~400 cross progeny hermaphrodites. In the control experiment, two Unc-101 hermaphrodites (that did not segregate any Unc-54 progeny) were observed in ~200 cross progeny. The coefficient of coincidence (C, the ratio of the observed frequency of double crossovers to the expected frequency) is 1.03 in *rec-1* homozygotes (taking the *dpy-5 unc-101* distance as 21 m.u. and the *unc-101 unc-54* distance as 4.6 m.u.) and 1.2 in control males (taking the *dpy-5 unc-101* distance as 12 m.u. and the *unc-101 unc-54* distance as 14 m.u.), indicating that there is no increase in double-crossing over in *rec-1* homozygous males when compared to wild-type controls.

***sDp1(I;f)* suppresses the *rec-1* phenotype:** ROSE and BAILLIE (1979b) found no linkage between *rec-1* and any markers located in the gene clusters of the autosomes, however, when markers located at the ends of the chromosomes were tested, *rec-1* showed loose linkage to *unc-54,* located on the right end of LG *I* (A. M. ROSE, unpublished results). Since *rec-1* is recessive to its wild-type allele (ROSE and BAILLIE 1979b; this study), a strategy to map the mutation was developed using two large free duplications of LG *I: sDp1(I;f),* covering the right two-thirds of the chromosome and *sDp2(I;f),* covering the left third (data shown in Table 4; extent of duplications shown in

TABLE 4

Duplication mapping of *rec-1*

Genotype	Wild types	Recombinants	pX100(C.I.)[a]
dpy-5 dpy-14 +/+ + rec-1	3238	28 Dpy-5	1.3 (0.88–1.8)
dpy-5 dpy-14 +/+ + rec-1/sDp1	1614	6 Dpy-5	1.6 (0.7–3.5)
dpy-5 dpy-14 rec-1/+ + rec-1	8659	321 Dpy-5	5.5 (5.4–5.6)
dpy-5 dpy-14 rec-1/+ + rec-1/sDp1	1201	5 Dpy-5	1.8 (0.7–4.1)
dpy-5 dpy-14 rec-1/+ + +	2213	25 Dpy-5	1.7 (1.1–2.4)
dpy-5 dpy-14 rec-1/+ + +/sDp2	1976	7 Dpy-5	0.7 (0.3–1.4)
dpy-5 dpy-14 rec-1/+ + rec-1	1729	67 Dpy-5	5.8 (4.4–7.2)
dpy-5 dpy-14 rec-1/+ + rec-1/sDp2	1002	13 Dpy-5	2.6 (1.3–4.2)
dpy-5 unc-13/+ +[b]	3119	34 Dpy 32 Unc	1.6 (1.2–2.0)
dpy-5 unc-13 +/+ + rec-1	2133	23 Dpy	1.6 (1.0–2.4)
dpy-5 unc-13 rec-1/+ + rec-1	3706	156 Dpy	6.25 (5.3–7.3)
dpy-5 unc-13 +/+ + rec-1/sDp2	1057	4 Dpy	0.2 (0.08–0.6)
dpy-5 unc-13 rec-1/+ + rec-1/sDp2	1977	41 Dpy	1.4 (0.9–1.9)

[a] C.I. = 95% confidence interval. See MATERIALS AND METHODS.
[b] Data from ZETKA and ROSE (1990).

Figure 2). Both duplications complement *dpy-5* and *dpy-14*. Although *sDp1* does pair and recombine with LG *I*, it does so rarely in the *dpy-5 dpy-14* region (ROSE *et al.* 1984; MCKIM *et al.* 1993), and in conjunction with the small size of this interval, it is unlikely that any of the recombinants recovered were the result of a crossover event with the duplication. In the absence of the duplication, the distance between *dpy-5* and *dpy-14* was 1.3 m.u. in *dpy-5 dpy-14 rec-1/+ + +* heterozygotes and increased to 5.5 m.u. in *rec-1* homozygotes. In the presence of *sDp1*, the frequency of exchange in the *dpy-5 dpy-14* interval was reduced giving a distance of 1.8 m.u. in *sDp1/dpy-5 dpy-14 rec-1/+ + rec-1* heterozygotes, a value not significantly different from that of 1.6 m.u. observed in *sDp1/dpy-5 dpy-14 + /+ + rec-1* heterozygotes. Thus, *sDp1* carried a wild-type allele of *rec-1*. The data are consistent with the finding that *rec-1* is completely recessive to its wild-type allele. To ensure that the suppression observed was not a general feature of LG *I* duplications, crossing over was also measured in the presence of *sDp2*. The distance measured between *dpy-5* and *dpy-14* in the presence of *sDp2* in *rec-1* mutants was 2.6 m.u., threefold higher than that of 0.7 m.u. observed in wild-type controls, indicating that the *rec-1* phenotype was expressed despite the presence of the duplication. Unlike *sDp1*, *sDp2* did not complement the high recombination phenotype. Although the frequency of crossing over in the presence of *sDp2* and *rec-1* was significantly higher than in controls, the distances were much lower than those obtained in the absence of the duplication (0.6 m.u. in *rec-1* homozygotes and 0.2 m.u. in heterozygotes). Fewer recombinants were recovered due to the presence of *sDp2*. This was tested using strains that were either heterozygous or homozygous for *rec-1*, in the presence and absence of *sDp2*, *i.e.*, *sDp2/dpy-5 unc-13 rec-1/+ + rec-1* and *sDp2/dpy-5 unc-13 +/+ + rec-1*. In the presence of *sDp2*, *(sDp2/dpy-5 unc-13/+ +)* the distance between *dpy-5* and *unc-13* decreased eightfold (1.6 to 0.2 m.u.); whereas in the presence of *sDp2* the *rec-1* distance decreased 4.5-fold (6.25 to 1.4 m.u.). In spite of the depression in map distance observed in the presence of *sDp2*, the Rec-1 mutant distance was sevenfold higher than wild type. Since the formula used to calculate the recombination frequency assumes that both *sDp1* and *sDp2* are inviable as a homozygotes, the results would be explained if *sDp2* homozygotes were recovered and

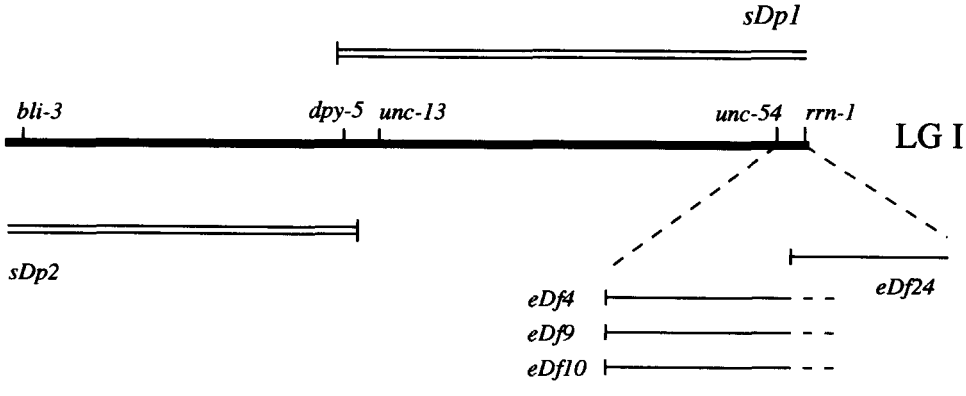

FIGURE 2.—A partial genetic map of chromosome *I* showing the relative positions of major markers and the breakpoints of rearrangements used in this study. The unlinked duplications *sDp1* and *sDp2* are shown by the unfilled bar and the deficiencies by a single line. *eDf4*, *eDf9* and *eDf10* fail to complement *unc-54* and complement the ribosomal deficiency *eDf24*, however their right breakpoints are unknown. *eDf24* is a partial deletion of the ribosomal cluster, *rrn-1* (ALBERTSON 1984).

TABLE 5

Deficiency mapping of *rec-1*

Genotype	Wild types	Recombinants	pX100(C.I.)[a]
unc-42 dpy-11/+ +	1250	26 Dpy 20 Unc	2.7 (2.0–3.6)
unc-42 dpy-11/+ +; rec-1/rec-1	1219	66 Dpy 59 Unc	7.6 (6.4–9.0)
unc-42 dpy-11/+ +; rec-1/eDf4	999	19 Dpy 23 Unc	3.1 (2.2–4.1)
unc-42 dpy-11/+ +; rec-1/eDf9	693	8 Dpy 11 Unc	2.0 (1.2–3.1)
unc-42 dpy-11/+ +; rec-1/eDf10	1127	29 Dpy	3.8 (2.5–5.4)
unc-42 dpy-11/+ +; +/eDf24	1668	35 Dpy 33 Unc	3.0 (2.3–3.8)
unc-42 dpy-11/+ +; rec-1/eDf24	2119	88 Dpy 72 Unc	5.6 (4.8–6.5)

[a] C.I. = 95% confidence interval. See MATERIALS AND METHODS.

reduced the number of recombinants observed. An alternative explanation is that *sDp2* suppresses recombination between the two homologues, however, there is no evidence for this (McKIM and ROSE 1990).

***eDf24(I)* fails to complement *rec-1*:** *rec-1* was suppressed by *sDp1*, which covers the right half of LG *I*, including most of the centrally located gene cluster. To map the *rec-1* gene, deficiencies near the right end of the chromosome were tested for failure to complement the mutation (data shown in Table 5). The deficiencies used in this study and their known breakpoints are shown in Figure 2. The *dpy-11 unc-42* interval, normally 2.7 m.u., increases to 7.6 m.u. in *rec-1* homozygotes. In *eDf24/rec-1; dpy-11 unc-42/+ +* heterozygotes, this interval showed a twofold enhancement in crossing over (5.6 m.u.) when compared to *eDf24/+; dpy-11 unc-42* controls (3.0 m.u.), indicating that the deletion failed to complement the *rec-1* mutation. *eDf24* had previously been used as a balancer to isolate a number of deletions of the *unc-54* locus (including *eDf4*, *eDf9*, *eDf10*, and *eDf13*) (ANDERSON and BRENNER 1984) that had undefined right breakpoints. Although these deficiencies genetically complemented *eDf24*, the physical endpoints are not known and the possibility remains that they physically overlap *eDf24* in a region not including any essential genes. The deficiencies tested complemented *rec-1*, with the possible exception of *eDf10*, which is outside the confidence interval for the *rec-1/+* control. However *eDf10* does not clearly fail to complement *rec-1*. This deficiency may overlap with *eDf24*, partially affecting *rec-1* function. Although *eDf24* significantly increases recombination frequency when heterozygous with *rec-1*, the increase is outside the confidence interval for the *rec-1* homozygote. Classically, (MULLER 1937) a shift toward the wild-type phenotype when placed over a deficiency is typical of a hypermorphic allele, however, there is no evidence for a semidominant phenotype in the case of Rec-1 (Table 4) (ROSE and BAILLIE 1979b). One might take the data as favoring a hypomorphic mutation, but because the phenotype involves the scoring of crossover frequencies, it is difficult to score large enough numbers that might resolve variation unambiguously. At present, the *rec-1* gene is identified by a single mutation that arose spontaneously, and the possibility that it produces an unpredictable neomorphic phenotype cannot be eliminated. Given the behaviour of *rec-1(s180)* in different genetic backgrounds, however, the likeliest explanation is that the mutation is an amorphic allele.

DISCUSSION

In many species, the distribution of meiotic exchanges is nonrandom with respect to physical length. The meiotic organization of the *C. elegans* chromosomes is optimal for examining the positioning of crossover events. The genetic length of chromosome *I* approaches 50 m.u. in hermaphrodites, corresponding to one crossover per meiosis (BRENNER 1974; ZETKA and ROSE 1990; reviewed in ZETKA and ROSE 1995) and facilitating investigation of where that crossover is most likely to occur. In the wild type, the medial portion of each autosome has a greatly reduced probability of an exchange relative to the flanking regions, resulting in the pronounced gene clusters observed on the genetic map (BRENNER 1974). Little is known about how, at the molecular level, the frequency of crossing over for different chromosomal locations is established. In this paper, we have described a mutation that alters the normal meiotic pattern of crossing over. The *rec-1* gene product appears to play a crucial role in determining the meiotic pattern of exchange events.

The *rec-1* mutation was initially identified as a recombination enhancer that increased meiotic crossing over in the autosomal clusters (ROSE and BAILLIE 1979b). In this study, the enhancement within the medial cluster was found to be interval specific, being more pronounced in the center of the cluster, around *unc-13*. Crossing over increased threefold in the *unc-11 dpy-5* interval and fivefold in the *dpy-5 unc-13* interval. A previous study showed similar expansions across these intervals after treatment with radiation (KIM and ROSE 1987). Furthermore, interval-specific enhancement was also observed for exchange frequencies in the male (ZETKA and ROSE 1990), consistent with the interpretation that the meiotic reduction in crossover frequency is most extreme in the center of the cluster. An early study correlating the genetic and physical maps be-

tween *dpy-5* and *unc-13* showed that the number of kb per map unit is greatest in the *dpy-14 unc-13* interval (STARR *et al.* 1989). The differential metric across the interval predicted by STARR *et al.* was used successfully to predict the physical position of the *bli-4* locus and facilitate its cloning (THACKER *et al.* 1995). Using the physical distances from BARNES *et al.* (1995), we calculated the number of kb per map unit. In wild type there are 1291 kb/m.u. in the *dpy-5 unc-13* interval compared to 740 kb/m.u. in the *unc-11 dpy-5* interval. In *rec-1* mutants, the difference between these intervals is less (327 compared to 254 kb/m.u.). Thus, the *rec-1* genetic background may be useful for predicting the physical location of a genetic locus. Our data show that *rec-1* reverses the recombination suppression normally present in the cluster and reduces the amount of difference between intervals.

The variation in the level of meiotic exchange is even more dramatic when intervals within the medial cluster are compared to regions outside the cluster. In wild type, for example, the *unc-101 unc-54* interval has 96 kb/m.u. There is an order of magnitude difference in the amount of exchange (from 1291 to 96 kb/m.u.) that is eliminated in the *rec-1* mutant (327 compared to 301 kb/m.u.). Furthermore, the amounts in *rec-1* homozygotes are similar to the genomic average of 333 kb per map unit. Thus, for the region of the chromosome defined by the markers *unc-11* and *unc-54*, the *rec-1* map is very similar to the physical map. These data support the interpretation that the *rec-1* mutant eliminates the meiotic pattern of crossing over.

Although the *rec-1* mutant can dramatically alter the probability of an exchange occurring in a certain interval, it does not affect the total number of exchanges. The result is a disruption of the normal distribution of crossovers (with no effect on viability or fertility). By determining the genetic distance across five intervals comprising most of chromosome *I*, we have shown that the genetic size of chromosome *I* in *rec-1* homozygotes approaches the 50 m.u. length observed in wild-type controls with no observable increase in double crossing over. In wild-type hermaphrodites (ZETKA and ROSE 1990), translocation heterozygotes (MCKIM *et al.* 1988, 1993) and inversion heterozygotes (ZETKA and ROSE 1992) the data indicates that even though crossing over may be restricted for large portions of the chromosome, a crossover occurs each meiosis in the available region. The significance of this has been investigated by crossover suppression along the length of the chromosome using two overlapping balancers, *hT2* and *hIn1*, thereby effectively eliminating crossing over on chromosome *I*. When this is done, the chromosome *I* homologues independently segregate (ZETKA and ROSE 1992), demonstrating that there exists a meiotic mechanism to ensure the formation of at least one crossover per bivalent every division and that the production of a meiotic exchange event is necessary for normal homologue disjunction. Mechanisms regulating the number of exchanges and the amount of interference appear to function normally in Rec-1.

We investigated the interaction between *rec-1* and two other genes affecting crossing over. Mutations in *him-6* (HODGKIN *et al.* 1979) and *him-14* (KEMPHUES *et al.* 1988; J. DUFFY and K. KEMPHUES, unpublished results) reduce crossing over leading to increased frequencies of nondisjunction for all the chromosomes. However, not all intervals have decreases in crossover frequencies. In fact, the distribution of exchanges for these mutants is quite similar to the distribution observed in the *rec-1* mutant, and increases in crossing over were observed for intervals within the gene cluster. However, unlike *rec-1, him-6* and *him-14* reduce the total amount of exchange along chromosome *I* to half the normal amount. These mutants are defective in both the frequency and distribution of meiotic exchange. In *him-6; rec-1* and *him-14; rec-1* homozygotes, a Him Rec phenotype is observed. The frequency of exchanges and nondisjunction approximates that observed in the Him mutants; whereas the distribution of exchanges approximates the Rec-1 distribution (with the possible exception of the *unc-13 unc-101* interval).

In the *rec-1* mutant, crossing over across the *bli-3 unc-11* interval to the left of the cluster, and *unc-13 unc-101* to the right, was not significantly different from the controls. The regions flanking the clusters are recombination promoting as defined by BARNES *et al.* (1995). One of these intervals, between *unc-13* and *unc-101*, has been reported to contain a recombination hotspot near the *mei-1* gene (CLARK-MAGUIRE and MAINS 1994). It seems unlikely that *rec-1* is specifically required for recombination at hotspots since the frequency across this interval did not decrease, although we cannot eliminate the possibility that a mutant decrease at the hotspot was compensated for elsewhere in the interval and averaged out to observed value. Crossing over in the *unc-101 unc-54* interval decreased significantly, and no evidence for a recombination hotspot in this region exists. We favor the interpretation that the *rec-1* gene product is involved in establishing the position of the exchange. The gene product might function in altering the chromatin structure, thus allowing recombination events to initiate in regions where they normally would not, or by altering the migration of the recombination apparatus, effectively randomizing the placement of the event. It is unlikely that *rec-1* is required for the exchange reaction itself, since the total number of events is normal. Exchange functions are more likely to be carried out by the *him-14* and *him-6* gene products, with *rec-1* determining where they are likely to occur.

In *S. cerevisiae* the genomic pattern of double-strand breaks (DSBs), commonly thought to be the substrate for the initiation of recombination (SUN *et al.* 1989; GAME 1992; ZENVIRTH *et al.* 1992), is nonrandom and DSBs cluster at specific sites or within short regions

(GAME 1992). The majority of DSBs are found near or at the promoter regions of transcribed genes and correlate strongly with the distribution of meiotic crossovers. In addition, DSB sites exhibit DNAse I hypersensitivity and are affected by changes in chromatin structure, indicating that an open chromatin conformation plays a role in determining the sites of meiotic recombination (OHTA *et al.* 1994; WU and LICHTEN 1994). However hotspot activity can be affected by sequences several thousand nucleotides away, suggesting that there is no one single hotspot-specific recognition factor involved in establishing recombination (WU and LICHTEN 1995). Although the basic mechanisms of meiotic exchange are likely to be conserved between yeast and *C. elegans,* there are a number of differences in the organization of the chromosomes. *C. elegans* chromosomes are less recombinogenic, for example, normally having only one exchange per bivalent (BRENNER 1974), and most exchange in *C. elegans* occurs in gene-poor regions (BARNES *et al.* 1995). Thus, the factors that determine the placement of crossovers may be different in yeast than in *C. elegans.*

A mutant phenotype of the Rec-1 type has not been described in other species. The control of crossover distribution has been analyzed in Drosophila, where mutations that alter the distribution of exchanges have been isolated (reviewed by BAKER *et al.* 1976). The majority of these mutations (including *mei-218, mei-S282,* and *mei-41*) are similar to *him-6* and *him-14* in that they reduce the frequency of crossing over and redistribute those crossovers that do occur (BAKER and CARPENTER 1972; PARRY 1973), and that they have been interpreted to be defective in a precondition necessary for exchange, possibly in site identification (BAKER *et al.* 1972; CARPENTER and SANDLER 1974). Mutations in *mei-9* reduce the frequency of exchange but maintain the normal pattern of events and conversely, mutations in *mei-352* maintain the normal frequency but disrupt the pattern of exchanges. CARPENTER (1979b) found that late recombination nodules in *mei-9* mutants were indistinguishable from those in wild-type in number and distribution, suggesting that mutants were capable of identifying sites for exchange but were unable to resolve a later step whereas the primary defect in *mei-352* mutants appears to lie in the ability to position the exchange events. In *mei-352,* the frequency of crossing over is increased in regions that are normally recombinationally suppressed, in the centric heterochromatin and on the fourth chromosome (BAKER and CARPENTER 1972; SANDLER and SZAUTER 1978). Mutations in *rec-1,* like *mei-9* and *mei-352,* functionally separate the control of crossover distribution from the control of exchange frequency. However, *rec-1* differs in two important respects. *mei-352* females are partially sterile, which cannot be explained by nondisjunction of the autosomes as a result of reduced recombination, since mutants have normal levels of exchange (BAKER and CARPENTER 1972). Mutants in *mei-352* exhibit increased nondisjunction and chromosome loss, however, this occurs at a frequency too low to explain the sterile phenotype (BAKER and CARPENTER 1972). Secondly, *mei-352* does not decrease the frequency of exchange in any interval. Thus, Rec-1 remains the sole mutant of its type in this unusual class of meiotic mutants.

We thank DAVID L. BAILLIE for his discussion and comments on the manuscript and KENNETH J. KEMPHUES for sharing strains and unpublished data. Some nematode strains used in this study were provided by the Caenorhabditis Genetic Center, which is funded by the National Institutes of Health National Center for Research Resources. This work was supported by a grant from the Natural Sciences and Engineering Council of Canada to A.M.R.

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Communicating editor: A. CHOVNICK