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Crossover and noncrossover recombination during meiosis: Timing and pathway relationships

AURORA STORLAZZI, LIUZHONG XU, LIANG CAO, AND NANCY KLECKNER*

Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA 02138

Contributed by Nancy Kleckner, April 27, 1995

ABSTRACT **During meiosis, crossovers occur at a high level, but the level of noncrossover recombinants is even higher. The biological rationale for the existence of the latter events is not known. It has been suggested that a noncrossover-specific pathway exists specifically to mediate chromosome pairing. Using a physical assay that monitors both crossovers and noncrossovers in cultures of yeast undergoing synchronous meiosis, we find that both types of products appear at essentially the same time, after chromosomes are fully synapsed at pachytene. We have also analyzed a situation in which commitment to meiotic recombination and formation of the synaptonemal complex are coordinately suppressed (*mer1* versus *mer1 MER2*$^{++}$). We find that suppression is due primarily to restoration of meiosis-specific double-strand breaks, a characteristic of the major meiotic recombination pathway. Taken together, the observations presented suggest that there probably is no noncrossover-specific pathway and that restoration of intermediate events in a single pairing/recombination pathway promotes synaptonemal complex formation. The biological significant of noncrossover recombination remains to be determined, however.**

During meiosis, recombinational interactions occur at high levels. Some interactions ultimately yield crossovers (CRs), but the majority are noncrossovers (NCRs) which do not result in exchange of flanking chromosome arms (e.g., see refs. 1–6). Crossovers, in combination with intersister connections, constitute chiasmata, which are essential for disjunction of homologs at the first meiotic division (7). The reasons for the existence and abundance of noncrossovers are not known. Two proposals have suggested the existence of a noncrossover-specific pathway devoted exclusively to chromosome pairing (3–5). Pairing interactions occur frequently along chromosomes (8) and would thus be more abundant than crossovers, which occur at a frequency of one to several per chromosome.

In yeast, one set of experimental observations could support the existence of a noncrossover-specific recombination pathway (9). In a *mer1* strain background, commitment to meiotic recombination in "return-to-growth" experiments and the level of crossovers in viable meiotic progeny are both reduced as compared with wild type, as is formation of synaptonemal complex (SC). Introduction of multiple copies of the *MER2* gene coordinately restores commitment to recombination and SC formation but not crossing-over. These suppression effects could be explained if the presence of extra *MER2* copies ("*MER2*$^{++}$") restored a noncrossover-specific pairing-specific recombination pathway.

More recently, evidence has been presented suggesting that chromosome pairing (i.e., physical juxtaposition of homologs) and recombination could be mediated by a single pathway of interhomolog interactions in which the two processes represent successive stages in a single series of events (e.g., see refs. 10–12). If a distinct noncrossover-specific pathway were found to exist, this hypothesis would be wrong.

Also of interest is the relationship of crossover and noncrossover recombination to cytologically observable interhomolog connectors, seen originally in *Allium* prior to SC formation (8) and also in yeast (13). Moreover, the relationship between crossovers and noncrossovers is central to an understanding of crossover interference, which is often thought to involve the designation of some recombination intermediates as crossovers with the remainder resolved as noncrossovers (e.g., see refs. 1, 14, 15).

To address these and other issues, we have developed a physical assay that monitors the formation of crossovers and noncrossovers individually and in real time during meiosis. We have used this assay, together with physical assays for intermediate events of meiotic recombination, to determine when noncrossover events occur during wild-type meiosis and to examine the nature of recombination in *mer1* and *mer1 MER2*$^{++}$ mutant strains.

MATERIALS AND METHODS

Strains. All strains are isogenic diploid derivatives of *Saccharomyces cerevisiae* SK1 (16, 17) homozygous for *ho*::*LYS2 lys2 ura3 leu2*::*hisG*. Additional markers in the strains used are as follows: NKY1551 is *his4XLEU2-MluI*::*BamHI URA3/his4BLEU2 arg4-nsp/arg4-bgl*. NKY2085 is *his4XLEU2-MluI*::*BamHI URA3/his4BLEU2-MluI trp1*::*hisG/trp1*::*hisG arg4-nsp/arg4-bgl*. NKY2203 and NKY2077 are the same as NKY2085 except that they are homozygous for *spo13*::*hisG* and contain, respectively, pRS424 (2μ *TRP1*) and pNKY456 (2μ *TRP1 MER2*). NKY2204 and NKY2078 are NKY2203 and NKY2077 also homozygous for *mer1*::*LEU2*. NKY1788 is NKY2085 also homozygous for *mer1*::*LEU2* and *ARG4* and contains *rad50S- KI81*::*ura3/rad50S-KI81*::*URA3*. Previous work describes markers on chromosome III (12, 17) and elsewhere (17, 19, 20); *mer1*::*LEU2* was introduced by transformation using pMEΔ162 (21) (= pOL139). pRS424 (= pOL142) is a derivative of pBluescript II (Stratagene) containing a yeast 2μ origin and *TRP1* (22). pNKY456 has the *Eco*RI–*Bam*HI *MER2* fragment from pME56 (= pOL141) (9) inserted into pRS424 between the *Eco*RI and *Bam*HI sites.

Tetrad Analysis Leading to CR/NCR Designations. All four-spore clones from 347 four-spore-viable tetrads of NKY1380 (relevant genotype in Fig. 2) were analyzed genetically for His, Leu, and Ura phenotypes and by restriction digestion for the status of all relevant *Xho* I, *Bam*HI, and *Mlu* I sites; cases of postmeiotic segregation were revealed by the latter analysis. In 320 tetrads, all detected events could be assigned as crossovers or noncrossovers unambiguously: 106 contained four parental spore clones; 67 contained no recombination of flanking markers but exhibited aberrant segregation at the central site I marker (5:3, 3:5, 6:2, or 2:6); 129 contained a single reciprocal

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Abbreviations: CR, crossover; NCR, noncrossover; SC, synaptonemal complex; DSB, double-strand break.

*To whom reprint requests should be addressed.

crossover between the outside markers with or without aberrant segregation at the central site I marker; 6 exhibited higher-order aberrant segregation in the absence of crossing-over (7:1 or 8:0); and 12 exhibited two reciprocal crossovers with or without aberrant segregation at the central marker. For the remaining 27 tetrads, only a small subset of the detected events could not be assigned unambiguously (not shown). The ambiguous cases represent 2% of 1388 chromosomes examined.

Meiotic Time Courses. Protocol 1 is described in ref. 12. Protocol 2: Stocks of cells, kept frozen at −80°C in 15% (vol/vol) glycerol, were thawed, grown for 16 hr on YP agar (23) supplemented with glycerol (3%) and adenine (50 mg/liter), and then streaked on synthetic complete medium lacking tryptophan [Trp drop-out medium (23)] to obtain single colonies. After 2 days, a single colony was inoculated in 25 ml of liquid Trp drop-out medium and grown with vigorous aeration for 24 hr. Cells were then collected by centrifugation, washed once in sterile water, diluted in liquid YP medium supplemented with acetate (1%) and adenine (50 mg/liter) to a final concentration corresponding to OD_{600} = 0.20, and incubated at 30°C with vigorous aeration for 12–13 hr. Cells were then collected and transferred into sporulation medium (23) to initiation meiosis (t = 0). Cell aliquots were withdrawn at desired times for DNA extraction and/or return to growth analysis.

DNA Analysis. DNA extraction, gel electrophoresis, transfer of fragments to nylon membranes, and visualization of fragments with radiolabeled probes are described elsewhere (12, 20). Probe B is a *Xho* I–*Bgl* II fragment of pNKY155; probe A is a *Bgl* II–*Pst* I fragment of pNKY291.

RESULTS

Assay System. Analysis of meiotic recombination in yeast has exploited physical assays that detect crossovers, branched recombination intermediates, double-strand breaks (DSBs), and formation of heteroduplex DNA in cultures of cells proceeding synchronously through meiosis (18, 24–31).

Our laboratory has applied such assays to a particular meiotic recombination hot spot, *HIS4LEU2*, which encodes two meiotic DSB sites, a major (site I) and a minor (site II) (Fig. 1). In one version of this locus, *HIS4LEU2-MluI*, site I comprises 77 bp of bacterial DNA that includes a *Mlu* I site near one edge; in a modified version, *HIS4LEU2-MluI::BamHI*, a 36-bp insertion of four *Bam*HI linkers is present at the *Mlu* I site. In both alleles, meiosis-specific DSBs occur relatively nonspecifically throughout an ≈175-bp region spanning the foreign DNA segment (12). Recombination has been assayed in diploid heterozygous both at site I (*Mlu/Mlu::BamHI*) and for appropriate flanking markers where heterozygosities are provided by *his4X* and *URA3* markers which eliminate *Xho* I cleavage sites.

A Physical Assay That Differentiates Between Crossovers and Noncrossovers. It is possible to identify specific DNA restriction fragments that arise specifically from crossovers or from noncrossovers at *HIS4LEU2* by digesting meiotic DNA with *Xho* I plus *Mlu* I and visualizing parental and recombinant fragments with either of two appropriate probes, A or B (Fig. 1).

The array of meiotic recombination products that arise at this locus has been determined by physical analysis of tetrad-containing spore clones produced by a strain like that in Fig. 1 (A.S., L.C., and N.K., unpublished results; *Materials and Methods*). Given this data set, for every fragment generated in a *Xho* I + *Mlu* I digest the fraction of molecules arising from a crossover or a detectable noncrossover—chromosome can be determined. Among the four recombinant fragments visualized by each probe, two arise almost exclusively from crossovers (R1 and R2 for both probes) and one arises exclusively from noncrossovers (R4 in the case of probe A; R3 in the case of probe B); the fourth fragment (R3 in the case of probe A and R4 in the case of probe B) represents a mixture of the two types of events, with noncrossovers predominating (Fig. 2). The two probes reveal two complementary sets of recombinant products.

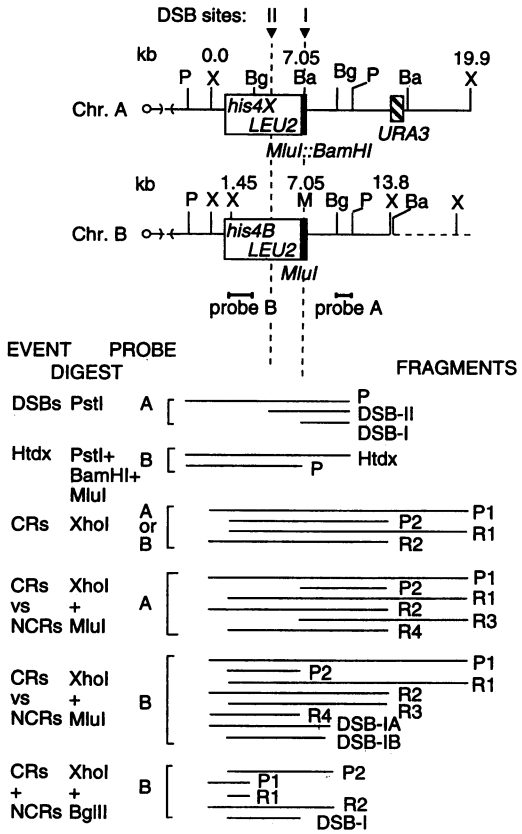

FIG. 1. Physical analysis of meiotic recombination at the *HIS4LEU2* locus. (*Upper*) The *HIS4LEU2* regions present on the two chromosomes III in most diploid strains analyzed. DSB sites (I and II) are indicated. Top and bottom chromosomes differ with respect to the allele at site I (*MluI::BamHI* or *MluI*) and with respect to flanking markers: to the right, the presence or absence of a *URA3* insert with concomitant absence or presence of a *Xho* I site; to the left, the presence or absence of the *his4X* allele with concomitant absence or presence of a *Xho* I site. Bottom chromosome is *his4B*. Restriction sites: Ba, *Bam*HI; Bg, *Bgl* II; M, *Mlu* I; P, *Pst* I; and X, *Xho* I. For *Bgl* II and *Pst* I, only relevant sites are given. (*Lower*) Physical assays for events of meiotic recombination. P, parental fragment(s); R, recombinant fragment(s).

The absolute levels of the eight recombinant fragments observed in meiotic DNA are as close to those predicted (Fig. 2) as can be expected, considering the low absolute levels of the species, significant background bands, the fact that 5–10% of cells never initiate meiosis, and the fact that DNA is not recovered with 100% efficacy from spores at late times.

A Physical Assay That Detects All Recombinational Interactions (Crossovers Plus Noncrossovers). Total recombinational interactions, crossovers plus noncrossovers, can be monitored by assaying a restriction fragment that represents the occurrence of recombination between "heteroalleles." In yeast, such recombinants virtually always involve aberrant (non 4:4) segregation at one of the markers, indicating the occurrence of a recombinational interaction in the immediate vicinity. With respect to markers flanking the pair of heteroalleles, such interactions may yield either crossovers or noncrossovers (32). Heteroallelic recombination was assayed using mutations *his4X* and *his4B*, which eliminate a *Xho* I site and a *Bgl* II site, respectively. A *HIS4* recombinant is detected by

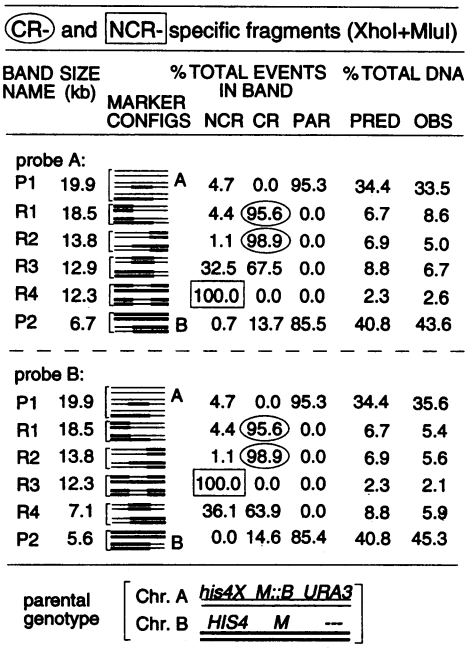

FIG. 2. crossover- and noncrossover-specific fragments in a *Xho* I + *Mlu* I digest. Restriction fragments that arise in wild-type meiosis specifically from crossover or noncrossover events have been identified (see text). For each restriction digest fragment generated by digestion with *Xho* I + *Mlu* I and visualized with the indicated probe, the percentage of total DNA molecules predicted to occur in that product (PRED) and the percentage of molecules contributed to that product by crossover-derived and noncrossover-derived chromosomes can be calculated. The parental marker configuration in NKY1380 is diagrammed at the bottom; the marker configurations that contribute to each fragment are indicated. The actual percentages of DNA molecules observed in each product (OBS) at a late time in meiosis are data from the wild-type time course in Fig. 4*B* (probe A; t = 8 hr) and from a second analogous wild-type time course (probe B; t = 8 hr). Most importantly, the two crossover-specific fragments are always several times more abundant than the noncrossover-specific fragments, as predicted.

appearance of a *Xho* I–*Bgl* II fragment characteristic of the wild-type gene (Fig. 1).

Noncrossovers Arise at the Same Time as Crossovers in Wild-Type Meiosis. A single synchronous meiotic culture has been examined by each of the assays described in Fig. 1. Events assayed previously occur with the expected timing (18, 27, 28). Crossover products as assayed by *Xho* I single digestion and heteroduplex DNA as assayed by digestion with *Pst* I + *Bam*HI + *Mlu* I are both barely discernible at t = 4 hr, clearly present at t = 5 hr, significantly more intense at t = 6 hr than at t = 5 hr, and slightly more intense at t = 7 hr than at t = 6 hr (Fig. 3*A* and *D*). DSBs are present at maximal levels ≈3 hr after transfer of cells to sporulation medium as seen in both the *Xho* I + *Bgl* II and *Xho* I + *Mlu* I digests (Fig. 3 *B* and *C*).

Crossovers and noncrossovers, as assayed by digestion with *Xho* I + *Mlu* I, arise coordinately, with timing identical to that observed for crossovers alone and heteroduplex DNA. This is shown for probe B (Fig. 3*B*) and seen in this same sample analyzed with probe A (not shown) and with both probes in other experiments (below; A.S., L.X., A. Schwacha, and N.K., unpublished data). The *Xho* I–*Bgl* II fragment representing the sum of crossovers and noncrossovers also exhibits appropriate timing. These much rarer products are first visible only at t = 5 hr and are somewhat more prominent at t = 6 and 7 hr (Fig. 3*C*).

Fragments diagnostic of crossover and noncrossover products probably represent completed recombination events.

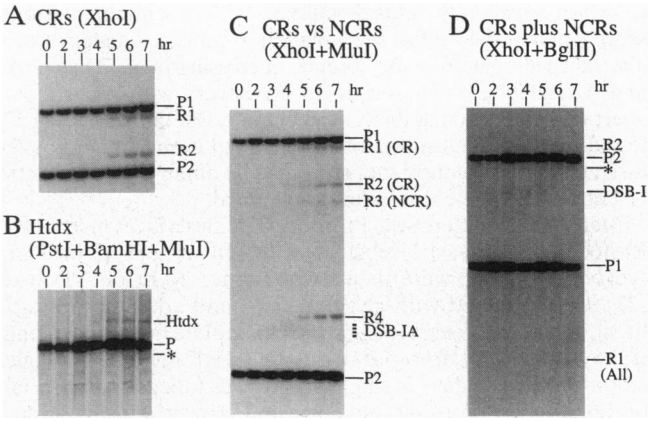

FIG. 3. Time course analysis of recombination-related events in a wild-type strain. NKY1551, a wild-type strain with *HIS4LEU2* markers as in Fig. 1, was analyzed for the four indicated types of recombination products by the appropriate digestion. Cells of a single culture were taken through synchronous meiosis (protocol 1). Meiosis was initiated by transfer of cells to sporulation medium (t = 0 hr) and DNA was isolated from samples taken at the indicated times thereafter. For the entire set of samples, aliquots were digested in parallel with each of the indicated restriction enzyme(s). The resulting fragments were then separated by agarose gel electrophoresis (0.6% in *A* and *C*; 0.8% in *B* and *D*), transferred onto a nylon membrane, and hybridized in all cases with probe B (Fig. 1). The origin of bands marked with * is unknown. Htdx, heteroduplex. In this particular culture, meiotic recombination events subsequent to DSBs occur slightly later (≈30 min) than typically observed for a wild-type strain under these conditions. For additional wild-type time course studies performed under analogous conditions, see Fig. 4 and other work (18, 27, 32).

Crossovers appear after heteroduplex DNA and close to the end of pachytene, which is the last point at which crossover formation can be disrupted (33), and noncrossover products also appear late. Furthermore, these fragments appear later than the one prominent recombination intermediate identified thus far (27).

Genetic Analysis of *mer1* and *mer1 MER2*$^{++}$ Strains. Among occasional viable progeny obtained from *mer1* mutant meiosis, the level of crossing-over is reduced about 10-fold. "Commitment to heteroallelic recombination" measured in a return-to-growth protocol is also reduced, 10-fold in the BR strain background originally characterized (9) and 15- to thirty-fold in the SK1 strain background analyzed here (Table 1). Introduction into a *mer1* strain of a multicopy plasmid encoding a wild-type *MER2* gene (*mer1 MER2*$^{++}$) restores essentially wild-type levels of commitment to heteroallelic recombination (ref. 9 and Table 1). The presence of extra *MER2* copies does not, however, restore meiotic crossing-over

Table 1. Commitment to heteroallelic meiotic recombination in wild-type and mutant SK1 strains

	Prototrophs × 10^4/total			
	his4XLEU2/ his4BLEU2		*arg4-Nsp/ arg4-Bgl*	
Genes	0 hr	5 hr	0 hr	5 hr
MER1	0.06	28 (≡1)	0.14	225 (≡1)
mer1	0.12	1.3 (0.05)	0.11	11 (0.05)
MER1 MER2^{++}	0.07	21 (0.75)	0.1	97 (0.43)
mer1 MER2^{++}	0.1	49 (1.75)	0.18	200 (0.9)

MER1 = NKY2203; *mer1* = NKY2204; *MER1 MER2*$^{++}$ = NKY2207; and *mer1 MER2*$^{++}$ = NKY2078. Heteroallelic recombination was measured by a standard return-to-growth protocol (20). Prototrophs/total = titer of colony-forming units on selective medium divided by titer of colony-forming units on selective medium supplemented with all essential nutrients.

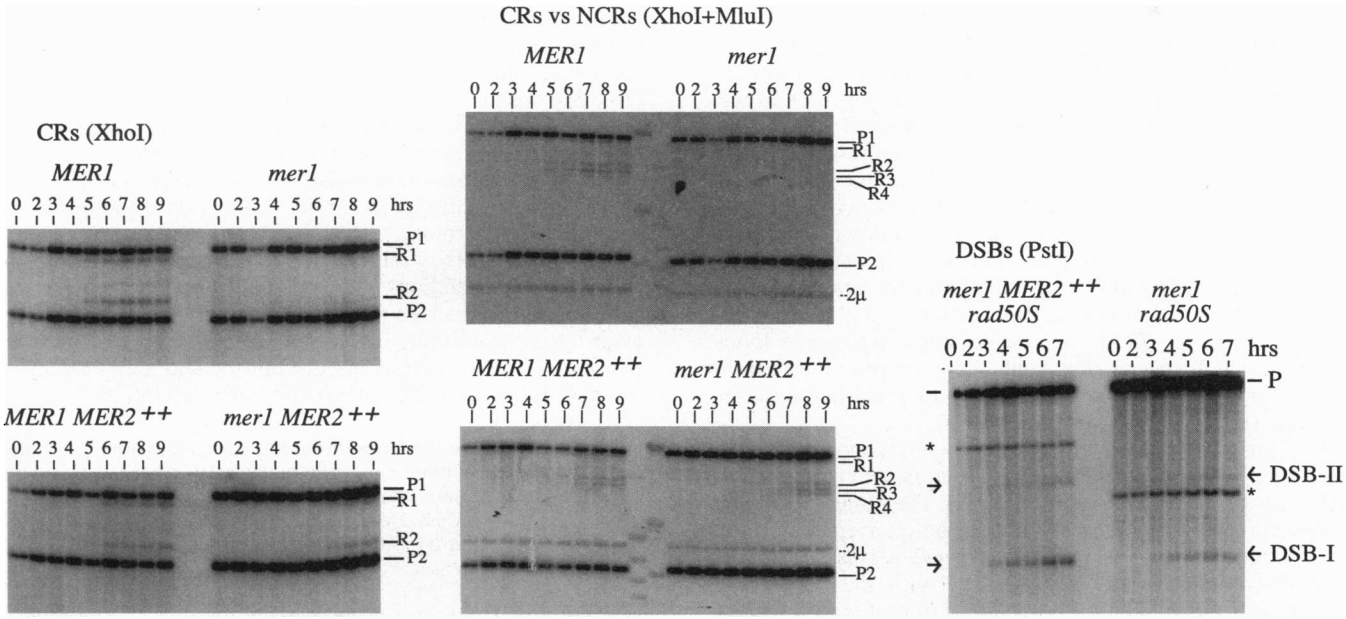

FIG. 4. Physical analysis of recombination-related events in *mer1* and *mer1 MER2*$^{++}$ mutants. Strains of the indicated genotypes were taken through synchronous meiosis (protocol 2); DNA was isolated and analyzed as in Fig. 3. *MER1* = NKY2203; *mer1* = NKY2204; *MER1 MER2*$^{++}$ = NKY2077; *mer1 MER2*$^{++}$ = NKY2078; *mer1 rad50S* = NKY1788/pRS424; *mer1 MER2*$^{++}$ *rad50S* = NKY1788/pNKY456. Meiosis is slightly slower in these experiments than in standard time course experiments because of the altered sporulation conditions used (*Materials and Methods*).

in viable meiotic progeny, which exhibit about one-tenth the wild-type level, as in *mer1* alone (9).

Physical Analysis of *mer1* and *mer1 MER2*$^{++}$ Strains. The physical assays described above have been applied to mer1 and mer1 MER2^{++} strains. Results are as follows:

(*i*) Crossing-over is strongly reduced in the *mer1* case. In a *Xho* I digest, crossover fragments are present at less than 20% the wild-type level; in *mer1 MER2*$^{++}$, however, crossing-over is higher than in *mer1*, about 30% of wild type (Fig. 4*A*). Thus, both strains show a defect in crossing-over in real time. The *MER2*$^{++}$ suppression effects, however, as revealed by this physical analysis, extend to crossovers as well as to other processes.

(*ii*) Noncrossover recombination is also strongly reduced in a *mer1* strain. All recombinant species in *Xho* I + *Mlu* I digests occur at very reduced levels (Fig. 4*B*). For probe A, the crossover-specific bands R1 and R2 are barely visible in the original autoradiogram and the noncrossover-specific band R4 is essentially invisible. This pattern suggests coordinate reduction in all events, which would predict that R4 should be less than a third as abundant as R1 and R2 (Fig. 2).

(*iii*) A *mer1 MER2*$^{++}$ strain is defective only in forming crossovers; noncrossovers occur apparently normally. In a *Xho* I + *Mlu* I digest of DNA extracted at t = 8 hr, the two crossover-specific species (R1 and R2) and the noncrossover-specific species (R4) are all present as about 2% of total DNA, approximately the same as for the noncrossover-specific species in *MER1* or *MER1 MER2*$^{++}$ at the same time point and approximately a quarter the level of the crossover-specific species in those strains at that time (Fig. 2). Once again it is apparent that the presence of the *MER2*$^{++}$ construct in the *mer1* strain increases the level of crossovers as well as of noncrossovers.

(*iv*) Meiosis-specific DSBs are defective in *mer1* and restored in *mer1 MER2*$^{++}$ as determined by analysis of strains that also carry the *rad50S* mutation, which causes breaks to accumulate in unresected form (19). In a *mer1 rad50S* strain, DSBs occur at ≈10% the level typically observed in a *MER1 rad50S* strain (1.3% vs. ≈15% at site I; 0.1% vs. ≈3% at site II). The level of DSBs in the *mer1 MER2*$^{++}$ situation is much higher than in *mer1*, essentially the same as in wild-type *rad50S* strains (11.9% vs. ≈15% at site I; 2.8 vs. ≈3% at site II) (Fig. 4*C*; *MER1 rad50S* results are from Table 1, probe 155 of ref. 12).

DISCUSSION

Crossover and Noncrossover Recombinants Appear at Essentially the Same Time During Meiosis. Most or all noncrossover recombinants are matured at about the same time as crossover recombinants. The current analysis would have detected 50% or more of noncrossover products that matured an hour or more before the rest. Thus, noncrossovers, like crossovers (28), are matured at or near the end of pachytene.

The Presence of Extra *MER2* Gene Copies in a *mer1* Strain Restores a DSB-Dependent Recombination Pathway. The deficit of commitment to gene conversion and of crossing-over reported previously from genetic analysis of a *mer1* mutant can now be attributed primarily to a deficit of meiosis-specific DSBs, which occur at a low level in this strain. Moreover, the suppression effects of extra *MER2* copies result largely from a restoration of DSBs to essentially normal levels. This increase is accompanied by a complete restoration of noncrossover events and a substantial but incomplete restoration of crossovers.

Chromosome Pairing. The results presented make it unlikely that there exists a separate noncrossover-specific recombination pathway. Such a pathway would have to yield noncrossover products which are matured at the same time as noncrossover products that arise by the normal pathway. Moreover, if the suppression effects of *MER2*$^{++}$ in a *mer1* strain were to represent the restoration of a second pathway, that pathway would have to involve DSBs.

Other observations have led to the suggestion that chromosome pairing and recombination represent successive manifestations of a single continuous series of interhomolog interactions (10–12). The absence of evidence for a noncrossover-specific pathway removes one important possible objection to this proposal.

Given the absence of evidence for a pairing-specific recombination pathway and evidence in favor of chromosome pairing via interactions that lead to recombination products, it now seems highly probable that the connector interactions ob-

served cytologically in *Allium* (8) do in fact correspond to recombinational interactions and, moreover, that they correspond to total recombinational interactions—i.e., to interactions that can ultimately yield either a crossover or a noncrossover, depending upon the outcome of other events.

Theoretically, some connectors might represent interhomolog interactions that are part of the single continuous pathway but yield neither crossovers nor noncrossovers. In yeast, at least, this seems unlikely. The number of interhomolog interactions in mitotic cells about to enter meiosis corresponds to the number of meiotic recombinational interactions (10); recombinational interactions are already rather frequent, one per 75 kb, or one per three pachytene loops; finally, a DNA species that might have represented such an interaction has now been shown to be a recombination intermediate (ref. 27 and unpublished data).

Cytologically observable interhomolog connectors have been seen in yeast thus far only in a mutant that lacks a major SC central region component, *zip1* (13). The number of visible connectors per *zip1* nucleus is about one-quarter the number of total recombinational interactions (≈45 versus ≈180–270). This discrepancy is not incompatible with the notion that pairing and recombination represent different manifestations of the same series of events. Perhaps, in yeast, only a subset of interhomolog interactions develop into this cytologically observable form; Sym and colleagues (13) have proposed, for example, that connectors might correspond only to crossover interactions. Alternatively, or in addition, however, morphological development of connectors into this visible form may be generally defective in a *zip1* mutant as compared to wild type. We favor this possibility. It is entirely plausible that Zip1 protein should be required to stabilize or mature interhomolog interactions, either concomitant with SC formation or by acting directly at the sites of interhomolog interactions irrespective of SC formation. Moreover, our recent observations demonstrate that the maturation of crossover recombination products is delayed several hours in a *zip1* mutant (A.S., L.X. and N.K., unpublished observations).

Restoration of SC Formation Results from Restoration of Recombination. A *mer1* BR strain usually forms full-length axial elements but no tripartite SC; a *mer1 MER2*$^{++}$ BR strain, in contrast, exhibits extensive SC formation, although the SCs are somewhat abnormal in appearance (9, 34). The same general tendency pertains in the SK1 background. In light microscope analysis (35), a *mer1* strain at midprophase contained silver-staining linearities that are always thinner than in wild type, while in a *mer1 MER2*$^{++}$ strain these linearities are qualitatively normal (data not shown).

The primary effect of the *MER2*$^{++}$ condition on recombination is an increase in the level of DSBs, which occur prior to and independent of the formation of SC (ref. 12, 28). It could have been the case that increased SC formation in the *MER2*$^{++}$ condition was the cause of the increased levels of recombination-related processes. The current observations strongly support the opposite view, that the increase in SC formation observed in the *mer1 MER2*$^{++}$ situation results from an increase in the quantity of appropriate recombinational interactions.

It is not clear how far along the pathway these interactions must progress to be effective in promoting SC formation. Full differentiation of intermediates into recombinant products does not appear to be essential: noncrossover products are not matured until the end of pachytene and, in *MER1 MER2*$^{++}$, most crossovers are not matured at all. The molecular events corresponding to commitment to gene conversion should be sufficient, as these are restored in *mer1 MER2*$^{++}$ strains. Formation of DSBs is necessary for commitment because the level of DSBs and the level of commitment are usually closely correlated; a DSB may not be sufficient, however.

In *Sordaria*, two meiotic mutants exhibit parallel decreases of aberrant segregations (i.e., total recombinational interactions), crossovers, late recombination nodules, and SC initiation sites (36). Perhaps the corresponding mutations decrease the number of interhomolog interactions formed at some early stage but not the maturation of those interactions once formed.

Why Do Noncrossovers Exist? Noncrossover recombinants are not effective in mediating the disjunction of homologs at meiosis I. Furthermore, although the abundance of noncrossover recombinants is related to the abundance of precursor DNA/DNA interactions involved in chromosome pairing, the occurrence of noncrossover recombination *per se* is not necessary for establishing a chromosome pairing interaction: pairing interactions occur in both mitotic and meiotic cells in the absence of exchange of genetic information (10, 12).

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