RECOMBINATION AND CHROMOSOME SEGREGATION DURING THE SINGLE DIVISION MEIOSIS IN *SPO12–1* AND *SPO13–1* DIPLOIDS[1]

SUE KLAPHOLZ[2] AND ROCHELLE EASTON ESPOSITO[2,3]

Committee on Genetics[2] and Department of Biology,[3] The University of Chicago, Chicago, Illinois 60637

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ABSTRACT

This paper reports a study of chromosome segregation and recombination during sporulation of *spo12–1* and *spo13–1* diploid strains of *S. cerevisiae*. These strains undergo a single division to form asci containing two diploid or near-diploid spores. The segregation of centromere-linked markers in the two-spored (dyad) products indicates that the division is generally equational. However, in a small percentage of the *spo12–1* and *spo13–1* cells, it appears that a meiosis I-like division occurs. Aberrant segregation of the *MAT* locus on chromosome *III*, yielding a monosomic and a trisomic spore pair, occurs in 12% of all dyads. The segregation patterns of markers at various distances from their centromeres and several pairs of markers on the same chromosome indicate that recombination takes place in both strains at nearly standard meiotic levels.

WHILE a large number of meiotic mutants have been characterized, few have been found that complete only one of the two meiotic divisions and form unreduced products. The study of such mutants has provided some insight into the genetic control of chromosome segregation, as well as regulation of each meiotic division (BAKER *et al.* 1976; GOLUBOVSKAYA 1979, for general reviews). In most mutants of this type, the majority of unreduced (diploid or near-diploid) products have been attributed to failure of the second meiotic division (ESEN, SOOST and GERACI 1979; JOHNSSON 1944; MOK and PELOQUIN 1972; RHOADES and DEMPSEY 1966; SATINA and BLAKESLEE 1935; STRINGHAM 1970; SCHILD and BYERS, personal communication). Very few mutants have been reported in which the meiosis I reductional division is absent and meiosis II takes place (LEVAN 1940; SMITH 1939).

Failure of chromosome segregation during either of the meiotic divisions is sometimes due to the presence of a large number of unpaired chromosomes during meiosis I. In several plant mutants defective in the establishment (asynaptic) or the maintenance (desynaptic) of pairing, cytological studies have revealed that only the first (JOHNSSON 1944; STRINGHAM 1970) or the second

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(LEVAN 1940) meiotic division takes place. For example, in two asynaptic mutants of Brassica, *as* and *as3*, light microscopy studies indicate that unpaired univalents generally undergo an equational centromere division during meiosis I. A second division is not observed, and diploid or near-diploid products are formed (STRINGHAM 1970). The occurrence of a single division during meiosis has also been attributed to the presence of mutations in genes involved in regulating entry into one of the divisions (BAKER *et al.* 1976; GOLUBOVSKAYA 1979). For example, in the dyad (*dy*) mutant of Datura, meiosis I proceeds normally, but the second meiotic division fails to occur (SATINA and BLAKESLEE 1935). The meiosis II equational centromere division is delayed until the first postmeiotic mitosis, and diploid spores are formed. In order to further our understanding of the genetic control of chromosome segregation and the regulation of the two meiotic divisions, we have investigated the behavior of two strains of yeast that undergo a single meiotic division.

In the preceding paper (KLAPHOLZ and ESPOSITO 1980), we described the isolation of the *spo12–1* and *spo13–1* alleles, each of which results in the production of two-spored asci, from *Saccharomyces cerevisiae* strain ATCC4117. ATCC4117 had previously been shown to form asci containing two diploid spores (GREWAL and MILLER 1972). Cytological examination of this strain led the authors to suggest that the single nuclear division was meiosis II (MOENS 1974; MOENS *et al.* 1977). However, a lack of genetic markers and the presence of a homothallism gene (*HO*) in the original strain (see KLAPHOLZ and ESPOSITO 1980) made it difficult to evaluate genetically whether meiosis I, meiosis II or some combination of these divisions occurs. Examination of individual *spo12–1* and *spo13–1* diploids during sporulation by staining the DNA with a fluorescent dye indicated that, as in ATCC4117, each strain undergoes a single division (KLAPHOLZ, unpublished). In order to study the properties of recombination and chromosome segregation in each of these strains, the *spo12–1* and *spo13–1* alleles were crossed into heterothallic (*ho*) genetic backgrounds, heterozygous for markers on a number of chromosomes. A genetic analysis of sporulation in the two strains is presented below.

Unlike most of the mutants described above, the majority of *spo12–1* and *spo13–1* cells undergo meiotic levels of recombination, followed by a single equational division. A small percentage of the two-spored products appear to result from a single reductional division. Aberrant segregation of chromosome *III*, resulting in approximately 12% monosomic and trisomic spore pairs, also occurs during sporulation of these strains. Hypotheses regarding the roles of the *spo12–1* and *spo13–1* alleles in meiosis and sporulation are evaluated in the DISCUSSION.

MATERIALS AND METHODS

Strains: The strains used in this study are listed with their genotypes and origins in Table 1.

Nomenclature: The symbols + and — designate dominant and recessive marker phenotypes, respectively. Mating phenotypes are indicated by the following symbols: N = nonmater, **a** = **a** mating type (mates with α testers only) and $\alpha = \alpha$ mating type (mates with **a** testers only). As in standard tetrad nomenclature, marker segregation in the two-spored asci is represented by the

TABLE 1

Genotype and origin of strains

Strain	Genotype	Origin
K215	*MAT***a** *lys2 tyr1 his7 TRP1 MET13 leu1* / *MATα lys2 TYR1 HIS7 trp1 met13 LEU1* *his6 lys7 ADE2 ARO7 spo13–1* / *HIS6 LYS7 ade2 aro7 spo13–1*	S. KLAPHOLZ
K216	*MAT***a** *tyr1 TRP1 ura3 CYH2 leu1 ade6* / *MATα TYR1 trp1 URA3 cyh2 LEU1 ADE6* *HIS6 lys1 met14 PET17 ARO7 spo12–1* / *his6 LYS1 MET14 pet17 aro7 spo12–1*	S. KLAPHOLZ
DH8–303	*MATα lys2 tyr1 HIS7 CAN1 URA3* / *MATα lys2 try1 his7 can1 ura3* *met13 cyh2 trp5 leu1 ade6 cly8 ade2* / *met13 CYH2 trp5 leu1 ADE6 CLY8 ade2*	D. PLOTKIN
DL171–477	*MAT***a** *LYS2 tyr1 his7 URA3* / *MAT***a** *lys2 tyr1 his7 ura3* *ADE5 met13 cyh2 trp5 leu1 ade6 cly8 ade2* / *ade5 met13 CYH2 trp5 leu1 ADE6 CLY8 ade2*	D. PLOTKIN

Gene symbols are as follows: *MAT***a** and *MATα* (or **a** and α), mating type; *ade*, adenine; *aro*, aromatic amino acids; *can*, canavanine resistance; *cly*, cell lysis; *cyh*, cycloheximide resistance; *his*, histidine; *leu*, leucine; *lys*, lysine; *met*, methionine; *pet*, petite; *spo*, sporulation-defective; *trp*, tryptophan; *tyr*, tyrosine and *ura*, uracil (cf. PLISCHKE *et al.* 1976).

format +: — spores for heterozygous recessive markers, and **a**:α:N spores for *MAT*. The phenotype of each member of a given dyad spore pair, for a particular locus, is represented by the format "phenotype of spore A, phenotype of spore B." For example, +, — indicates spore A has a + phenotype and spore B has a — phenotype.

Media: All media have been previously described (KLAPHOLZ and ESPOSITO 1980).

Genetic techniques: The genetic procedures employed in this study have been described (KLAPHOLZ and ESPOSITO 1980).

Calculation of second-division segregation frequencies: Second-division segregation (SDS) frequencies were determined by standard techniques, using one or more markers closely linked to their centromeres (*ade1*, *met3*, *met14*, *pet8* and *trp1*) to establish the first-division segregation pattern of each ascus (MORTIMER and HAWTHORNE 1969). An average of 60 tetrads with 4 viable spores from several Spo+ control crosses were used to calculate the SDS frequencies presented in Tables 5 and 6.

Determination of the genotypes of mating-capable ascosporal clones: In order to determine the genotypes of K215- and K216-derived **a** and α ascosporal clones, they were mated with genetically marked *MATα/MATα* (DH8–303) and *MAT***a**/*MAT***a** (DL171–477) diploid testers (Table 1), respectively. One hybrid colony from each cross was sporulated and 10 to 20 4-spored asci dissected. The segregation of *MAT* and recessive markers on chromosomes *II*, *V*, *VII* and *XV* was examined in these asci. Tetrad types diagnostic of various spore clone genotypes are presented in Table 2. Crosses involving spore clones that are heterozygous (+/—) or hemizygous (+/O) wild type, or homozygous (—/—) or hemizygous (—/O) recessive, for a given marker, will generate the same ascus types. However, in some instances, these genotypes can be distinguished by examining the segregation of another marker on the same chromosome that was originally homozygous wild type in the parental K215 or K216 diploid, and is homozygous recessive in the diploid tester, *e.g.*, *trp5* (chromosome *VII*). This additional marker, either +/O

TABLE 2

Marker segregation in tetrasomic and trisomic hybrids

Cross genotype*			Expected tetrad types (+ :-)†			
Spore clone	×	Diploid tester	4:0	3:1	2:2	1:3
+/+		—/—	+	+	+	
		+/—	+	+		
+/—		—/—			+	+
		+/—	+	+	+	
+/*O*		—/—			+	+
		+/—	+	+	+	
—/—		+/+	+	+	+	
		+/—			+	+
—/*O*		+/+	+	+	+	
		+/—			+	+

* Crosses between K215 and K216 ascosporal clones and diploid testers, DL171–477 and DH8–303 (Table 1).

† Tetrad types expected from tetrasomic segregation are from ROMAN, PHILIPS and SANDS (1955), and those expected from trisomic segregation assuming trivalent pairing are from SHAFFER *et al.* (1971).

or +/+ in the ascosporal clone, depending upon whether the chromosome is present in 1 or 2 copies, will exhibit trisomic (+/—/—) or tetrasomic (+/+/—/—) segregation (Table 2). Trisomic marker configurations in the spore clones are not detected by this procedure.

Tetrad types diagnostic of monosomy or disomy for the *MAT* locus in the spore clones are shown in Table 3. The cross hybrid will exhibit trisomic segregation if the **a** or α clone is monosomic, and tetrasomic segregation if the clone is disomic.

Determination of genotypes of nonmating ascosporal clones: The genotypes of nonmating (N) sporulation-capable ascosporal clones were analyzed by sporulating and dissecting 20 or more dyads from each clone. Segregation of both + and — progeny spores indicates a heterozygous genotype; segregation of only + progeny spores indicates a +/+ or a +/O genotype. In

TABLE 3

MAT *segregation in tetrasomic and trisomic hybrids*

Cross genotype*			Expected tetrad types (**a**:α:N)†								
Spore clone	×	Diploid tester	0:0:4	1:1:2	2:2:0	2:0:2	2:1:1	3:1:0	0:2:2	1:2:1	1:3:0
a/**a**		α/α	+	+	+						
a/*O*		α/α			+				+	+	+
α/α		**a**/**a**	+	+	+						
a/*O*		**a**/**a**			+	+	+	+			

* Crosses between **a** and α K215 and K216 ascosporal clones and α/α and **a**/**a** diploid testers, DH8–303 and DL171–477 (Table 1).

† Tetrad types expected from **a**/**a**/α/α tetrasomic segregation are from ROMAN, PHILLIPS and SANDS (1955), and those expected from **a**/**a**/α and **a**/α/α trisomic segregation assuming trivalent pairing are from SHAFFER *et al.* (1971). The following asci with only three viable spores are diagnostic of **a**/**a**/α/α tetrasomy (0:0:3), **a**/**a**/α trisomy (3:0:0 and 2:0:1) and **a**/α/α trisomy (0:3:0 and 0:2:1).

some instances, the segregation of other heterozygous markers on the same chromosome can be used to distinguish homozygous from hemizygous genotypes. Trisomic marker configurations (+/+/— or +/—/—) are not detected by this procedure. The analysis of *MAT* segregation among the progeny spores is described in RESULTS.

RESULTS

The behavior of several genetic markers closely linked to their centromeres, as well as markers located at various distances from their centromers, was used to analyze chromosome segregation and recombination during sporulation of *spo12–1* and *spo13–1* homozygous diploids. The genotypes of the strains employed in this study, K215 (*spo13–1*) and K216 (*spo12–1*), are given in Table 1. Both strains produced approximately 65% asci at 30°, more than 99% of which contained only two spores (dyads).

The majority of cells undergo an equational division: The genetic consequences of a single reductional (meiosis I) or equational (meiosis II) sporulation division are shown in Table 4. During a reductional division, a heterozygous recessive marker (+/—) closely linked to its centromere will segregate 1:1 to yield two homozygous spores (+/+ and —/—). In contrast, an equational diviison will generate two heterozygous (+/—) spores. A single recombinational event between a heterozygous recessive marker and its centromere, followed by an equational division will result in half 2:0 and half 1:1 dyads. When a single recombinational event is followed by a reductional division, only 2:0 dyads are formed.

The segregation of heterozygous recessive markers in 84 *spo12–1* (K216) and 100 *spo13–1* (K215) dyads is summarized in Tables 5 and 6, respectively. (The data for the *MAT* locus are presented separately in a later section.) Spore viability was 88% for K216 and 73% for K215. The following conclusions were drawn from the individual marker segregation data presented in Tables 5 and 6: (1) Only two classes of dyads with two viable spores were observed for each marker, 2:0 and 1:1. The absence of 0:2 dyads rules out the possibility that extensive chromosome loss or haploidization takes place in either strain. (2) The majority dyad class for all markers, linked and unlinked to their centromeres, is 2:0, demonstrating that most chromosomes divide equationally. (3) With increasing gene-centromere distance, the proportion of 1:1 dyad phenotypes increases as

TABLE 4

Genetic consequences of reductional and equational chromosome segregation in strains that undergo a single division during sporulation

	No exchange		Single exchange	
Chromosome segregation	Phenotype of dyad	Genotypes of spores	Phenotype of dyad	Genotypes of spores
Reductional	1:1	+/+,—/—	2:0	1/2 +/—,+/—
Equational	2:0	+/—,+/—	1/2 1:1	1/2 +/—,+/—
			1/2 2:0	1/2 +/—,+/—

TABLE 5

Segregation of heterozygous markers in K216 spo12–1 *dyads*

Chromosome:	Marker	Dyad phenotypes*					1:1 dyads	Gene-centromere distance‡	
		2:0	1:1	1:0	0:1	Total	Total†	1/2 SDS	cM
IV	*trp1*	65	4	14	1	84	0.06	<0.01	1
VII	*leu1*	64	5	11	4	84	0.07	0.03	3
XI	*met14*	61	8	15	0	84	0.12	<0.01	3
V	*ura3*	59	10	14	1	84	0.15	0.07	7
IX	*his6*	52	17	13	2	84	0.25	0.15	14
XV	*pet17*	51	18	13	2	84	0.26	0.28	17
XVI	*aro7*	50	19	15	0	84	0.28	0.26	25
IX	*lys1*	47	22	13	2	84	0.32	0.33	29
VII	*ade6*	48	21	14	1	84	0.30	0.36	32
VII	*cyh2*	46	23	13	2	84	0.33	0.42	59
II	*tyr1*	46	22	12	3	83	0.32	0.35	120

* No 0:2 dyads were observed.
† Total = dyads with two viable spores only (2:0 plus 1:1).
‡ Gene-centromere distances were measured in tetrad-producing diploid strains. SDS (second-division segregation) frequencies were derived from control cross tetrads (see MATERIALS AND METHODS), except for *trp1* (MORTIMER and HAWTHORNE 1966). Control map distances are from MORTIMER and HAWTHORNE (1975); cM = centiMorgans.

TABLE 6

Segregation of heterozygous markers in K215 spo13–1 *dyads*

Chromosome:	Marker	Dyad phenotypes*					1:1 dyads	Gene-centromere distance‡	
		2:0	1:1	1:0	0:1	Total	Total†	1/2 SDS	cM
IV	*trp1*	57	3	38	2	100	0.05	<0.01	1
VII	*leu1*	47	13	36	4	100	0.22	0.03	3
IX	*his6*	41	19	33	7	100	0.32	0.15	14
XVI	*aro7*	48	12	35	5	100	0.20	0.26	25
XIII	*lys7*	36	21	34	6	97	0.36	0.23	27
XV	*ade2*	40	20	30	10	100	0.33	0.34	68
VII	*met13*	33	26	32	8	99	0.44	0.38	80
II	*tyr1*	40	20	34	6	100	0.33	0.35	120
II	*his7*	41	19	28	12	100	0.32	0.33	168

* No 0:2 dyads were observed.
† Total = dyads with two viable spores only (2:0 plus 1:1).
‡ Gene-centromere distances were measured in tetrad-producing diploid strains. SDS (second-division segregation) frequencies were derived from control cross tetrads (see MATERIALS and METHODS), except for *trp1* (MORTIMER and HAWTHORNE 1966). Control map distances are from MORTIMER and HAWTHORNE (1975); cM = centiMorgans.

expected from recombination followed by an equational division. (4) There is no obvious bias in the recovery of + and − spores from dyads with only one viable spore. Thus, spore death does not appear to be correlated with recombinational or segregational events on a particular marked chromosome.

In both strains, *trp1* is the most closely linked centromere marker, located less than 1 centiMorgan (cM) from the centromere of chromosome *IV* (MORTIMER and HAWTHORNE 1975). In approximately 95% of both *spo12–1* and *spo13–1* dyads with two viable spores, *trp1* exhibited 2:0 segregation, indicating that approximately 95% of the sporulating cells undergo an equational division.

A single reductional division occurs in less than 5% of sporulating cells: The number of dyads in which *trp1* segregated 1:1 (4 of 69 *spo12–1* and 3 of 60 *spo13–1*) sets a limit of approximately 5% on the proportion of the *spo12–1* and *spo13–1* dyad populations that undergo a single reductional division. This is an upper limit because 1:1 segregation for *trp1* could also be due to events confined to the *trp1* locus or chromosome *IV*. These would include gene conversion or gene-centromere recombination at an unexpectedly high level prior to an equational division, and reductional or aberrant segregation of chromosome *IV* alone (Figure 1).

If the 5% 1:1 *trp1* dyads are the result of a reductional division of the entire genome, they should also show reductional segregation for *leu1*, 3 cM from the centromere on chromosome *VII*. This proved to be true for three of the four *spo12–1*, and one of the three *spo13–1* dyads in which *trp1* segregated 1:1.

In the three *spo12–1* dyads, coincident 1:1 segregation for all four of the closest centromere-linked markers, *trp1*, *leu1*, *met14* and *ura3*, was observed (Table 7). The complete phenotypes of these dyads and their expected frequencies are presented in Table 8. Note that in one of these dyads, K216–80, one locus on each of the nine genetically marked chromosomes showed 1:1 segregation.

In the one *spo13–1* dyad, all markers less than 25 cM from their centromers, and three additional markers with greater gene-centromere distances, exhibited 1:1 segregation. The frequency with which a dyad of this particular phenotype was expected to arise by chance (*i.e.*, the product of the 2:0 or 1:1 frequencies of each marker presented in Table 6, corrected for linked markers) is 1000-fold less than that observed (expected $= 1.4 \times 10^{-5}$; observed $= 1.7 \times 10^{-2}$). The simplest interpretation is that this dyad resulted from a single meiosis I-like division of the genome. The 2:0 segregation patterns of the four other markers (*aro7*, *lys7*, *tyr1* and *his7*) located 25 or more cM from their centromers would then be due to gene-centromere recombination followed by reductional segregation (Table 4). These results indicate that approximately 2% of the *spo13–1* and 4% of the *spo12–1* cells undergo a single reductional division.

Two additional *spo12–1* dyads were observed in which only two of the four closest centromere-linked markers exhibited 1:1 segregation (Table 7). The complete phenotypes and expected frequencies of these dyads are presented in Table 8 (classes VI and VII). These dyads raise the possibility that during a

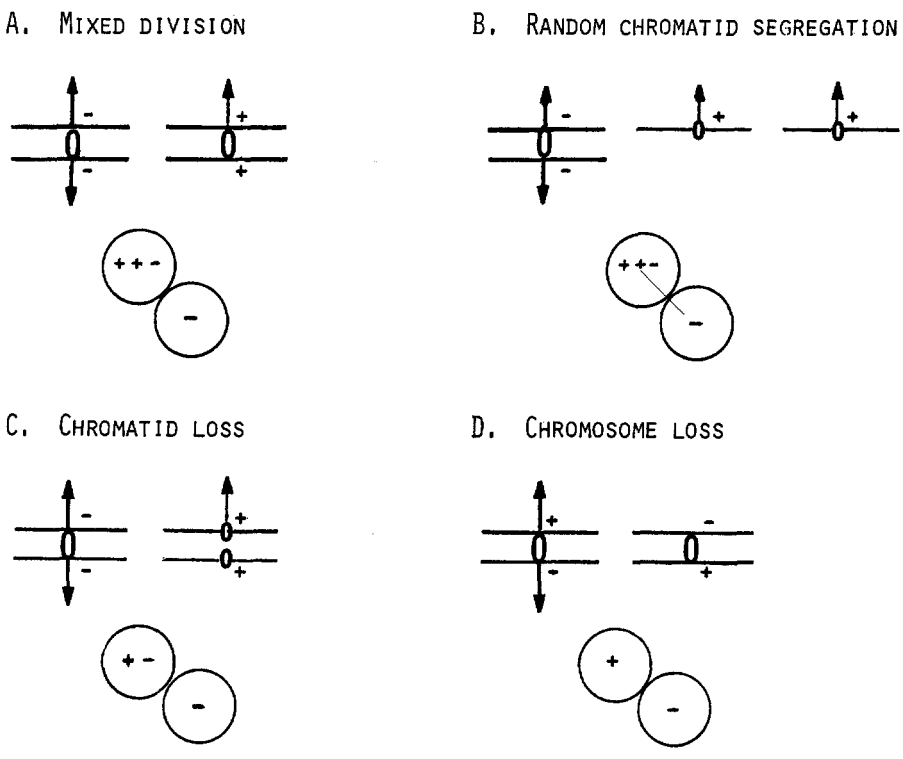


FIGURE 1.—Several aberrant segregational events that could result in 1:1 dyad formation. (A) Mixed division: One homolog fails to divide and segregates at random to one of the two poles. (B) Random chromatid segregation: One homolog undergoes a precocious centromere division, resulting in the random segregation of two chromatids. (C) Chromatid loss: Failure of one chromatid to pass to either of the two poles. (D) Chromosome loss: Failure of one chromosome to segregate. Note that in order to generate a 1:1 dyad, the chromosome that divided equationally must be recombinant. If the homologs were nonrecombinant, 2:0 or 0:2 monosomic spore pairs would be formed.

Note that 2:0 dyads, in which one spore is + monosomic, could also be formed *via* events A, B and C.

single division, some chromosomes divided equationally and others divided reductionally (see DISCUSSION).

Evidence that intergenic recombination is responsible for most 1:1 dyads: Direct evidence for the occurrence of recombination followed by equational division comes from the behavior of markers on the same chromosome. For all pairs of linked markers in the *spo12–1* and *spo13–1* strains (except *tyr1* and *his7*, both of which are not centromere-linked), the centromere proximal markers had lower 1:1 segregation frequencies than did the distal markers (*e.g.*, *leu1* = 0.07, *cyh2* = 0.33, Table 5; *leu1* = 0.22, *met13* = 0.44, Table 6). Furthermore, changes in coupling, indicative of one or more recombinational events, occurred between all marker pairs (Table 9). For example, dyad phenotypes B and C

TABLE 7

Coincident 1:1 marker segregation in spo12–1 *dyads*

Class	Dyad phenotype*				Number observed	Percent of total
	leu1	*met14*	*trp1*	*ura3*		
I	2:0	2:0	2:0	2:0	53	76.8
II	1:1	2:0	2:0	2:0	2	2.9
III	2:0	1:1	2:0	2:0	4	5.8
IV	2:0	2:0	1:1	2:0	0	0
V	2:0	2:0	2:0	1:1	5	7.2
VI	2:0	1:1	2:0	1:1	1	1.5
VII	2:0	2:0	1:1	1:1	1	1.5
VIII	1:1	1:1	1:1	1:1	3	4.4

* The segregation patterns of the four closest centromere-linked markers in 69 K216 dyads are presented. None of the other possible phenotypes were found. *leu1* = 3cM, *met14* = 3cM, *trp1* = 1cM, and *ura3* = 7cM from their respective centromeres (MORTIMER and HAWTHORNE 1975).

for the *tyr1-his7* pair, which comprise 58% of the total dyads, each require at least one recombinational event.

If all 1:1 spore pairs resulted from meiotic levels of recombination followed by equational division (Table 4), their frequency should equal half the second-division segregation (SDS) frequency of each marker. The SDS frequency measured in control tetrads is equal to twice the gene-centromere distance for markers within 33 cM of the centromere and reaches a theoretical maximum of 67% for more distal (unlinked) markers.

The SDS frequencies measured in control tetrads (MATERIALS AND METHODS) are presented for comparison with the 1:1 dyad frequencies of *spo12–1* and *spo13–1* in Tables 5 and 6, respectively. The frequency of 1:1 dyads for markers less than 15 cM from their centromeres was between two and 12 times higher than half the SDS frequency in the control. With increasing gene-centromere distance, the 1:1 dyad frequencies approached half the SDS frequencies. Unlinked markers (> 33 cM) showed an average of 72% SDS in control cross tetrads and 35% 1:1 segregation in *spo12–1* and *spo13–1* dyads. These results suggest that the level of recombination in both dyad-producing strains is close to that observed in tetrad-producing strains.

The larger deviation from the expected 1:1 dyad frequency for markers closely linked to their centromeres than for more distal markers is attributable, in part, to reductional segregation. For the closely linked centromere markers, both the observed and the "expected" (based on half the control SDS frequency) numbers of 1:1 dyads are relatively small. Thus, a small percent of "reductional dyads" can account for a large proportion of the total 1:1 dyads. For example, three of the five *spo12–1* dyads in which *leu1* exhibited 1:1 segregation (Table 7) are reductional (see Table 8). When these reductional dyads are omitted from the total, the 1:1 frequency becomes equal to half the SDS frequency (2 of 66 = 0.03).

TABLE 8

Phenotypes of K216 spo12–1 *dyads exhibiting coincident 1:1 segregation for centromere markers*

Class*	Dyad number	Chromosome:	Phenotype of spore A, Phenotype of spore B												Expected frequency‡
			II	*III*	*IV*	*V*	*VII*			*IX*		*XI*	*XV*	*XVI*	
		marker:	*tyr1*	*MAT*	*trp1*	*ura3*	*ade6*	*leu1*	*cyh2*	*his6*	*lys1*	*met14*	*pet17*	*aro7*	
		cM†:	120	25	1	7	32	3	59	14	29	3	17	25	
VIII	12		+,+	N,N	+,—	—,+	+,+	—,+	+,—	—,+	+,+	+,—	—,+	+,+	3.0×10^{-7}
	45		+,+	α,N	+,—	—,+	+,+	—,+	—,+	—,+	+,+	—,+	+,+	+,+	6.3×10^{-8}
	80		+,—	**a**,α	+,—	+,—	+,+	—,+	+,+	+,+	—,+	+,—	—,+	—,+	1.4×10^{-7}
VI	38		—,+	**a**,α	+,+	—,+	+,+	+,+	—,+	+,+	+,+	—,+	+,+	—,+	4.6×10^{-5}
VII	13		—,+	N,N	—,+	—,+	+,—	+,+	+,+	—,+	+,+	+,+	+,—	—,+	3.8×10^{-6}

* Refers to classification in Table 7 based upon the segregation of the four closest centromere-linked markers, *trp1*, *leu1*, *met14* and *ura3*.

† Gene-centromere distance (MORTIMER and HAWTHORNE 1975).

‡ The expected frequency for each complete dyad phenotype is equal to the product of the individual 1:1 or 2:0 (+:—) and 1:1:0, 0:0:2 or 0:1:1 (**a**:α:N) frequencies for each marker (Tables 5 and 10), corrected for linked markers. The observed frequency is $1/69 = 1.5 \times 10^{-2}$ for each dyad.

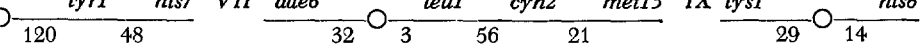
TABLE 9

Evidence for recombination in spo12–1 *and* spo13–1*:segregation of markers on the same chromosome*

Phenotypic class	Dyad phenotypes: Proximal marker Spore A	Proximal marker Spore B	Distal marker Spore A	Distal marker Spore B	Number of dyads in each phenotypic class for linked markers*: Gene pair:	*leu1-met13*	*tyr1-his7*	*leu1-cyh2*	*leu1-ade6*	*his6-lys1*
					Parental coupling	+ −	+ +	+ −	+ +	+ −
A	+	+	+	+		27 (46%)	23 (38%)	42 (61%)	43 (62%)	33 (48%)
B	+	+	+	−		19 (32%)	17 (28%)	22 (32%)	21 (30%)	19 (28%)
C	+	−	+	+		6 (10%)	18 (30%)	3 (4%)	5 (7%)	14 (20%)
D	+	−	+	−		4 (7%)	2 (3%)	1 (1%)	0	1 (1%)
E	+	−	−	+		3 (5%)	0	1 (1%)	0	2 (3%)

leu1-met13 and *tyr1-his7* are from K215 (60 total dyads); *leu1-cyh2*, *leu1-ade6* and *his6-lys1* are from K216 (69 total dyads).

* The meiotic map positions (in cM) are as follows (MORTIMER and HAWTHORNE 1975):



A small percent of reductional dyads are not expected to affect significantly the number of 1:1 dyads observed for markers not linked to their centromeres for two reasons (1) the number of reductional dyads is relatively small compared to the total number of 1:1 dyads, and (2) the centromere-unlinked markers often exhibited 2:0 segregation in the reductional dyads due to recombination (see Table 8).

Since a number of aberrant segregational events, as well as gene conversion, could also generate 1:1 dyads (see Figure 1), a genotypic examination of the ascosporal clones was undertaken.

2:0 marker segregation reflects two heterozygous genotypes: If 2:0 marker segregation reflects a single equational division or a reductional division following exchange, both spores should be heterozygous (Table 4). Similarly, if 1:1 marker segregation is due to an equational division following exchange, or a reductional division, the spores should be homozygous. These predictions were tested by analyzing the genotypes of *spo12–1* and *spo13–1* ascosporal clones.

A total of 20 ascosporal clones from 11 *spo12–1* dyads, including five clones from the three reductional dyads shown in Table 8 (class VIII), and 18 ascosporal clones from nine *spo13–1* dyads, were examined. In both strains, the heterozygous mating-type locus (*MAT***a**/*MAT*α) segregated to a yield three phenotypic classes of spores: **a** mating type (**a**) α mating type (α) and nonmating (N) sporulation-capable (described below). The genotypes of markers on chromosomes *II*, *III*, *V*, *VII* and *XV* in 21 **a** and α spore clones were analyzed by crossing to marked diploid testers; the complete genotypes of 17 N clones

were examined by sporulation and dyad dissection. These procedures are detailed in the MATERIALS AND METHODS section. It was not always possible to make an unambiguous assignment of genotype to each marker examined in a given ascosporal clone.

For markers that exhibited 2:0 segregation in the 38 ascosporal clones, a total of 70 *spo12–1* and 56 *spo13–1* individual marker genotypes were determined. In 98% of the cases, 2:0 marker segregation indicated that the spore clones were heterozygous, as expected. The data for two markers are summarized below. The centromere-linked marker *leu1* was heterozygous in 13 of 14 *spo12–1* and 10 of 10 *spo13–1* spore clones. Similarly, all *spo12–1* (6 of 6) and *spo13–1* (7 of 7) spore clones were heterozygous for *tyr1*, located 120 cM from its centromere (MORTIMER and HAWTHORNE 1975). Two of the 20 *spo12–1* ascosporal clones examined appeared to be aberrant in genotype (*i.e.*, either homozygous or hemizygous wild type) for one or two markers that exhibited 2:0 segregation; they are being investigated further.

While our methods of analysis would not have distinguished spore clones that were heterozygous for a particular marker from those that were trisomic (+/—/—) (see MATERIALS AND METHODS), the presence of a significant number of trisomic spore clones is unlikely because: (1) no +/O monosomic spore clones, the reciprocal products of trisomic spore clones (see Figure 1), were identified, and (2) in most cases, the genotypes of both members of a dyad could be assigned, and both appeared to be heterozygous.

1:1 marker segregation may indicate two homozygous spores or an aberrant genotype: For markers that exhibited 1:1 segregation, a total of 33 (17 + and 16 —) *spo12–1* and 22 (13 + and 9 —) *spo13–1* individual marker genotypes were determined. This sample included 13 genotypes of markers from the *spo12–1* reductional dyads. In all of the *spo12–1* dyads examined, 1:1 marker segregation indicated that the spore clones were homozygous, as expected.

In contrast to these results, four of the nine *spo13–1* dyads examined were aberrant in genotype for one or two markers that exhibited 1:1 segregation. All of the spore clones that were recessive in phenotype for *leu1* (4 of 4), *met13* (3 of 3) and *tyr1* (2 of 2) proved to be homozygous, as expected. However, approximately half of the spore clones that were wild type in phenotype for these markers were found to be aberrant in genotype, either hemizygous or heterozygous: *leu1* (2 or 4), *met13* (1 of 3) and *tyr1* (2 of 3). In addition, all three + clones were homozygous for *ADE2*.

These results demonstrate that 1:1 marker segregation, at least in the *spo13–1* dyads, is caused in some proportion of the cases by events other than gene-centromere recombination followed by an equational division or reductional segregation alone. For example, the chromosome *VII* genotypes of the two *spo13–1* dyads in which *leu1* and/or *met13* segregated aberrantly are as follows: (1) spore A *leu1/LEU1 met13/MET13*, spore B *leu1/leu1 met13/met13*, and (2) spore A *leu1/LEU1 met13/MET13*, spore B *leu1/leu1 met13/MET13*. The first dyad could have originated by gene conversion of both *LEU1* to *leu1* and *MET13* to *met13*, and the second by a single conversion of *LEU1* to *leu1*. Gene conver-

sion during sporulation of *spo12–1* and *spo13–1* strains has been demonstrated for several heteroallelic loci, including *leu1* and *met13*, and appears to be elevated (KLAPHOLZ, unpublished). The former dyad could also have resulted from loss of one chromosome *VII* chromatid from spore B, and subsequent restoration to disomy, since chromosome *VII* monosomics are generally unstable (BRUENN and MORTIMER 1970; PARRY and ZIMMERMAN 1976). We are further investigating this finding in *spo12–1* and *spo13–1* strains with markers that will allow us to distinguish between the different possible causes of 1:1 marker segregation. The next section presents evidence that aberrant segregation of the *MAT* locus in *spo12–1* and *spo13–1* dyads is due largely to abnormal chromosome segregation.

Aberrant phenotypic segregation is observed for the MAT *locus:* The mating type (*MAT*) locus is located 25 cM from the centromere on chromosome *III* (MORTIMER and HAWTHORNE 1975). Because the two alleles, *MAT***a** and *MAT*α, are co-dominant, this locus has been particularly useful in the phenotypic detection of aberrant chromosome segregation (described below). Strains that contain one or more copies of either *MAT***a** (**a** mating type) or *MAT*α (α mating type) can be distinguished from one another and from heterozygous *MAT***a**/*MAT*α (nonmating) strains by their unique mating behavior. The segregation of *MAT* in the *spo12–1* and *spo13–1* dyads is shown in Table 10.

Consistent with our conclusion that the majority of cells undergo an equational division, most dyads contained two nonmating (N) spores. The expectation that these spores were *MAT***a**/*MAT*α in genotype was confirmed by sporulating and dissecting eight clones from 0:0:2 dyads. The segregation of mating phenotypes in the dyads produced by these ascosporal clones (Table 11) was similar to that observed in the dyads produced by the parental *MAT***a**/*MAT*α diploids, K215 and K216 (Table 10).

The second most frequent type of dyad produced by both strains contained one spore of **a** mating type and one of α mating type (Table 10). Spore pairs of this sort were expected to arise primarily from gene-centromere recombination followed by an equational division, and thus be *MAT***a**/*MAT***a**, *MAT*α/*MAT*α in genotype. The level of 1:1:0 dyads produced by *spo12–1* (39%) and *spo13–1* (27%) was consistent with this view; 27% *MAT*-centromere recombination was observed in control cross tetrads. All crosses involving six pairs of **a** and α spore clones from 1:1:0 dyads and *MAT*α/*MAT*α or *MAT***a**/*MAT***a** diploid testers exhibited tetrasomic segregation patterns for *MAT* (see Table 3), indicating that the *spo12–1* and *spo13–1* spore clones were *MAT***a**/*MAT***a** or *MAT*α/*MAT*α in genotype (Table 12).

Two other types of dyads, not expected to occur by either reductional or equational segregation, were found at a moderately high frequency; 1:0:1 and 0:1:1 dyads constituted 7% of the *spo12–1* and 17% of the *spo13–1* dyads (Table 10). There are three genetically distinguishable ways in which such dyads could have arisen: (1) chromatid loss, (2) aberrant chromatid segregation, and (3) gene conversion. The genetic consequences of each event are shown in Table 13.

TABLE 10

Segregation of mating phenotypes in spo12–1 *and* spo13–1 *dyads*

Strain	Dyads with 2 viable spores (a : α : N)*					Dyads with 1 viable spore (a : α : N)†				Total spores		
	0:0:2	1:1:0	1:0:1	0:1:1	Total	0:0:1	1:0:0	0:1:0	Total	a	α	N
K215: *spo13–1* / *spo13–1*	34 (57%)	16 (27%)	7 (12%)	3 (5%)	60	29 (73%)	6 (15%)	5 (13%)	40	29	24	107
K216: *spo12–1* / *spo12–1*	37 (54%)	27 (39%)	2 (3%)	3 (4%)	69	10 (67%)	2 (13%)	3 (20%)	15	31	33	89

* No 2:0:0 or 0:2:0 dyads were observed.

† The number of 0:0:1, 1:0:0 and 0:1:0 dyads obtained approximates that expected from random spore death: 26, 8 and 6 for K215 and 9, 3 and 3 for K216, respectively.

TABLE 11

MAT *genotypes of N spore clones from 0:0:2, 1:0:1 and 0:1:1 dyads*

Strain	No. spore clones	Mean % spore viability	*MAT* segregation in dyads from sporulation of N spore clones: Dyad phenotypes (a:α:N)* 0:0:2	1:1:0	1:0:1	0:1:1	0:0:1	1:0:0	0:1:0	Total spores a	α	N
Dyad type 0:0:2												
K215	4	68	16	9	5	5	30	7	4	21	18	69
K216	4	88	58	16	1	2	17	1	2	18	20	136
Percent of total†			66.1	22.3	5.4	6.3						
Dyad type 1:0:1												
K215	3	57	14	1	1	7	13	0	2	2	10	49
K216	1	62	21	1	0	11	29	0	4	1	16	84
Percent of total†			62.5	3.6	1.8	32.1						
Dyad type 0:1:1												
K215	2	64	13	1	5	1	12	6	0	12	2	44
K216	3	69	32	2	10	1	24	1	1	9	2	60
Percent of total†			69.2	4.6	23.1	3.1						

Nonmating ascosporal clones from 0:0:2, 1:0:1 and 0:1:1 dyads were sporulated and 20 or more dyads were dissected from each clone.

* There is no apparent correlation between spore death and the phenotype of the surviving spore.

† Percent of total K215 and K216 dyads with two viable spores.

TABLE 12

MAT *genotypes of* **a** *and* α *spore clones from 1:1:0, 1:0:1 and 0:1:1 dyads*

Strain	No. spore clones	Mating type	*MAT* segregation in crosses to a/a or α/α testers: Mean % spore viability	Tetrasomic a/a/α/α	Trisomic a/a/α	Trisomic a/α/α	Tri- or Tetrasomic*	Total spores a	α	N	Inferred genotype
Dyad type 1:1:0											
K215	2	**a**	69	9	0	0	1	5	4	46	**a/a**
K216	4	**a**	63	16	0	0	7	20	20	81	**a/a**
K215	2	α	76	8	0	1	6	8	12	40	α/α
K216	4	α	80	20	0	0	9	18	22	81	α/α
Dyad type 1:0:1											
K215	3	**a**	63	0	0	12	9	11	50	34	**a**/o
K216	1	**a**	83	0	0	6	0	2	14	14	**a**/o
Dyad type 0:1:1											
K215	2	α	74	1	11	0	6	47	16	21	α/o
K216	2	α	88	1	12	0	4	31	11	24	α/o
	1	α	84	15	0	0	2	11	12	47	α/α

The **a** and α ascorporal colonies were crossed to α/α and **a**/**a** diploid testers, respectively, and 10 to 20 four-spored asci from each cross hybrid were dissected (see MATERIALS AND METHODS). The inferred genotype is based upon the segregation of mating phenotypes in asci with three or four viable spores and the overall **a**:α:N spore ratio. The ascal types diagnostic of **a**/**a**/α/α tetrasomic segregation (ROMAN, PHILLIPS and SANDS 1955), and **a**/**a**/α and **a**/α/α trisomic segregation assuming trivalent pairing (SHAFFER *et al.* 1971) are shown in Table 3. The **a**/**a**/α/α tetrasomics are expected to produce **a**:α:N spores in a 1:1:4 ratio (ROMAN, PHILLIPS and SANDS 1955), and **a**/**a**/α and **a**/α/α trisomics, in approximately 3:1:2 and 1:3:2 ratios, respectively (HABER 1974).

* Nondiagnostic ascus types (see Table 3).

TABLE 13

Genetic consequences of aberrant chromosome behavior and gene conversion on MAT *segregation during a single sporulation division*

Segregation or recombination event	Segregation of *MAT* in dyads: No exchange — Phenotype of dyad*	No exchange — Genotypes of spores	Single exchange — Phenotype of dyad*	Single exchange — Genotypes of spores
Chromatid loss:				
Reductional division	1:1:0	1/2 **a**/**a**,α 1/2 **a**,α/α	1/2 1:0:1 1/2 0:1:1	1/2 **a**,**a**/α 1/2 α,**a**/α
Equational division	1/2 1:0:1 1/2 0:1:1	1/2 **a**,**a**/α 1/2 α,**a**/α	1/4 1:0:1 1/4 1:1:0 1/2 1:1:0	1/4 **a**,**a**/α 1/4 α,**a**/α 1/4 **a**,α/α 1/4 **a**/**a**,α
Aberrant segregation:				
Mixed division†	1/2 1:0:1 1/2 0:1:1	1/2 **a**,**a**/α/α 1/2 α,**a**/**a**/α	same as no exchange	
Random chromatid segregation‡	1/4 1:0:1 1/4 0:1:1 1/2 0:0:2	1/4 **a**,**a**/α/α 1/4 α,**a**/**a**/α 1/2 **a**/α,**a**/α	1/4 1:0:1 1/4 0:1:1 1/4 1:1:0 1/4 0:0:2	1/4 **a**,**a**/α/α 1/4 α,**a**/**a**/α 1/4 **a**/**a**,α/α 1/4 **a**/α,**a**/α
Gene conversion§:	1/2 1:0:1 1/2 0:1:1	1/2 **a**/**a**,**a**/α 1/2 α/α,**a**/α	same as no exchange	

* **a**:α:N spores.

† One homolog divides equationally; the other segregates as a unit to one of the two poles (see Figure 1).

‡ One homolog divides equationally; the other undergoes precocious centromere division, resulting in the random segregation of two chromatids (Figure 1).

§ Assumes *MAT***a** converts to *MAT*α and *MAT*α converts to *MAT***a** with equal frequency.

The evidence presented below demonstrates that these exceptional dyads were generally the result of aberrant chromatid segregation.

Most **a** *and* α *clones from 1:0:1 and 0:1:1 dyads are monosomic for the* MAT *locus:* The **a** and α spore clones from 1:0:1 or 0:1:1 dyads were expected to be monosomic (**a**/*o* or α/*o*), if the dyads resulted from aberrant chromatid segregation or loss (Table 13). On the other hand, gene conversion of *MAT***a** to *MAT*α or *MAT*α to *MAT***a** would be expected to generate *MAT*α/*MAT*α, *MAT***a**/*MAT*α and *MAT***a**/*MAT***a**, *MAT***a**/*MAT*α diploid spore pairs, respectively (Table 13). To distinguish between gene conversion and the other two mechanisms, crosses were made between four **a** and five α clones from 1:0:1 and 0:1:1 dyads and the *MAT*α/*MAT*α or *MAT***a**/*MAT***a** diploid testers. Trisomic mating-type segregation (see Table 3) was observed in eight of nine crosses, demonstrating that the spore clones were monosomic for the *MAT locus* (Table 12). This result eliminated gene conversion as the primary explanation for the 1:0:1 and 0:1:1 dyads.

Tetrasomic mating-type segregation was observed in one cross, indicating that the spore clone K216–45A contained two copies of *MAT*α (Table 12). Genotypic

analysis of its sister (N) spore (described in the next section) suggested that K216–45A was originally monosomic for chromosome *III* and became disomic during growth.

N clones from 1:0:1 and 0:1:1 dyads are generally trisomic for MAT: The N clones from 1:0:1 and 0:1:1 dyads were expected to be heterozygous *MAT***a**/*MAT*α if dyads of this phenotype result from chromatid loss (Table 13). If aberrant chromatid segregation were responsible for generating the exceptional dyads, the N clones should be trisomic for *MAT* (Table 13). In the former case, the frequency of each type of dyad produced by these N clones should be the same as those produced by N clones from 0:0:2 dyads.

The expected genetic consequences of disomy or trisomy for *MAT* in strains that undergo a single meiotic division are presented in Table 14. While the phenotypic outcome of an equational division without recombination is the same for spore clones of either ploidy, all other segregational events have different consequences. In *MAT***a**/*MAT***a**/*MAT*α or *MAT***a**/*MAT*α/*MAT*α trisomics, it is expected that a large proportion of the 1:1:0: dyads that are formed by *MAT***a**/*MAT*α diploids will be replaced by 1:0:1 or 0:1:1 dyads, respectively. Furthermore, 0:1:1 dyads are expected to be produced by a *MAT***a**/*MAT***a**/*MAT*α clone only if aberrant segregation occurs; likewise for 1:0:1 dyads from a *MAT***a**/*MAT*α/*MAT*α clone (data not shown). However, in *MAT***a**/*MAT*α clones, aber-

TABLE 14

Dyad types expected from sporulation of N diploid and trisomic spore clones

Chromosome segregation	Spore clone genotype	No exchange		Single exchange	
		Phenotype of dyad†	Genotypes of spores	Phenotype of dyad†	Genotypes of spores
Equational	**a**/α	0:0:2	**a**/α,**a**/α	1/2 1:1:0	1/2 **a**/**a**,α/α
				1/2 0:0:2	1/2 **a**/α,**a**/α
	a/**a**/α	0:0:2	**a**/**a**/α,**a**/**a**/α	1/3 1:0:1	1/3 **a**/**a**/**a**,**a**/α/α
				2/3 0:0:2	2/3 **a**/**a**/α,**a**/**a**/α
	a/α/α	0:0:2	**a**/α/α,**a**/α/α	1/3 0:1:1	1/3 α/α/α,**a**/**a**/α
				2/3 0:0:2	2/3 **a**/α/α,**a**/α/α
Reductional	**a**/α	1:1:0	**a**/**a**,α/α	0:0:2	**a**/α,**a**/α
	a/**a**/α	1/3 1:1:0	1/3 **a**/**a**/**a**,α/α	1/9 1:1:0	1/9 **a**/**a**/**a**,α/α
		2/3 1:0:1	2/3 **a**,**a**/**a**/α/α	4/9 1:0:1	4/9 **a**,**a**/**a**/α/α
				4/9 0:0:2	4/9 **a**/α,**a**/**a**/α
	a/α/α	1/3 1:1:0	1/3 **a**/**a**,α/α/α/α	1/9 1:1:0	1/9 **a**/**a**,α/α/α/α
		2/3 0:1:1	2/3 α/α,**a**/**a**/α/α	4/9 1:0:1	4/9 α/α,**a**/**a**/α/α
				4/9 0:0:2	4/9 **a**/α,**a**/α/α/α

* The following assumptions were made in calculating the dyads expected from the trisomic strains: (1) a single exchange event is equally likely between any two of the three homologs, and (2) trivalent pairing occurs with random 2 from 1 disjunction. The relevant phenotypic consequences of aberrant segregation are discussed in the RESULTS.

† **a**:α:N spores.

rant segregational events are expected to generate both exceptional dyad types in equal frequency (Table 13).

As is shown in Table 11, the summed frequencies of the different dyad classes generated by sporulation of N clones derived from 0:0:2, 1:0:1 and 0:1:1 dyads are very different. The data suggest that at least some of the N clones from 1:0:1 and 0:1:1 dyads are *MAT***a**/*MAT*α/*MAT*α and *MAT***a**/*MAT***a**/*MAT*α trisomics, respectively. For example, two clones that closely fit the expectations for *MAT***a**/*MAT*α/*MAT*α trisomy and *MAT***a**/*MAT***a**/*MAT*α trisomy, respectively, are K216–47B and K216–54A. While the N clones from K216 0:0:2 dyads generated an average of 20.7% 1:1:0: dyads from a sample of 77 dyads with two viable spores, 47B produced only 3.0% (33 total) and 54A only 4.2% (24 total) 1:1:0 dyads. Trisomic strains are expected to produce very few 1:1:0 dyads because such dyads result only from reductional segregation (1/3 of the no-exchange plus 1/9 of the single-exchange products, Table 14) and aberrant segregation. The N clones from K216 0:0:2 dyads produced an average of 1.3% 1:0:1 and 2.7% 0:1:1 dyads. In contrast, 47B produced no 1:0:1 and 33.3% 0:1:1 and 54A, 29.1% 1:0:1 and no 0:1:1 dyads. The relatively large percentage of only one type of exceptional dyad is indicative of trisomy (Table 14). Thus, aberrant chromatid segregation, with no loss of genetic material, appears to be the mechanism responsible for generating exceptional dyads. Two types of events that could result in a three-from-one chromatid distribution, "mixed" division and precocious centromere division followed by random chromatid segregation (Figure 1; Table 13), are considered in DISCUSSION.

DISCUSSION

Yeast strains homozygous for either of the recessive alleles, *spo12–1* or *spo13–1*, produce almost exclusively two-spored asci (dyads) during sporulation (KLAPHOLZ and ESPOSITO 1980). Genetic analysis of chromosome segregation and recombination in each diploid strain has demonstrated the following: (1) the spores contain diploid or near-diploid genomes, (2) approximately 95% of the dyads result from a single equational division, (3) a few percent of the dyads result from a single reductional division, (4) recombination takes place at or close to standard meiotic levels and (5) aberrant segregation of chromosome *III* occurs in approximately 12% of dyads.

Chromosome segregation is regulated at both the cellular and the individual chromosomal level: Although only one division takes place during sporulation of *spo12–1* and *spo13–1*, the mode of chromosome segregation is not fixed, *i.e.*, the division is generally equational, but it may be reductional. A similar phenotype has been reported in another mutant that sometimes undergoes a single division during meiosis, the elongate (*el*) mutant of maize (NEL 1975). The segregation of centromere markers indicates that most of the unreduced meiotic products result from a single reductional division (RHOADES and DEMPSEY 1966; NEL 1975). However, NEL (1975) observed that approximately 20% of the diploid eggs result from a single division in which at least one chromosome divided

equationally. The presence of only one marked chromosome in NEL's study prevented the author from determining whether the "decision" to divide equationally was made at the level of the cell or the individual chromosome.

In some instances, segregational behavior does appear to be regulated at the level of the individual chromosome. A number of mutants that exhibit chromosome-specific effects on loss or nondisjunction during meiosis have been reported in Drosophila (see BAKER and HALL 1976, for review). In yeast, HABER (1974) and LIRAS *et al.* (1978) described a recessive mutation, *chl*, that causes nonrandom mitotic chromosome loss. In our study of chromosome segregation in *spo12–1* and *spo13–1* diploids, coincident 1:1 phenotypic segregation for some, but not all, centromere-linked markers was observed at frequencies too high to be explained by meiotic levels of recombination (*e.g.*, see Table 8). These dyads can be explained as the result of a single meiotic division in which some chromosomes segregated equationally, others reductionally. Alternatively, the level of recombination in these cells may be greatly elevated in near-centromere regions, as has been observed in meiotic mutants of Drosophila and other organisms (BAKER *et al.* 1976).

More convincing evidence that chromosome segregation may be partially regulated at the level of the individual chromosome comes from the analysis of *MAT* segregation in *spo12–1* and *spo13–1* dyads. Abberrant segregation of the *MAT* locus on chromosome *III*, independent of whether the majority of chromosomes divided equationally or reductionally, occurred frequently in both strains (Table 10). The finding that most of the exceptional dyads (1:0:1 and 0:1:1) contained one spore that was monosomic and one that was trisomic for *MAT* (Tables 11 and 12) suggested that a three-from-one chromatid distribution of chromosome *III* had taken place. The segregation of both *MAT* and *leu2*, located on the opposite side of the centromere from *MAT*, in other *spo12–1* and *spo13–1* strains supports this conclusion (KLAPHOLZ, unpublished). This type of aberrant chromosome distribution could result from (1) a "mixed" division in which one univalent does not divide and segregates at random to one of the two poles, while its homolog equationally, or (2) a precocious centromere division followed by random chromatid segregation (Figure 1; Table 13). Both types of abnormal chromosome behavior have been described in a number of meiotic mutants. The occurrence of an equational division of some univalents and random segregation of others has been reported in asynaptic and desynaptic plant mutants (PRAKKEN 1943; SOOST 1951; STRINGHAM 1970). Precocious centromere division, often resulting in random segregation of chromatids at anaphase II without further division, has been observed in several meiotic mutants in plants (CLAYBERG 1959; LAMM 1944; JOHNSSON 1944) and Drosophila (DAVIS 1971; MASON 1976).

Is aberrant segregation limited to specific chromosomes? The amount of aberrant segregation that other chromosomes undergo was difficult to assess in the present study. This is, in part, because the products of aberrant segregation of chromosomes marked with heterozygous recessive markers are not phenotypically unique as they are for *MAT* (see Figure 1). Genotypic analysis of 38 ascosporal clones revealed that 98% of the markers that exhibited 2:0 segrega-

tion were heterozygous, as expected. However, approximately one-third of the markers in *spo13–1* that exhibited 1:1 segregation were aberrant in genotype, *i.e.*, heterozygous or hemizygous in the + spore. Thus, while gene conversion or aberrant segregational events appear to be responsible for some of the 1:1 dyads (at least for *spo13–1*), it is not possible from these data to estimate the extent of their contribution to the total 1:1 dyad types for each marker and obtain a corrected measure of gene-centromere recombination and aberrant segregation.

The excess in 1:1 dyad types over that expected from recombination plus reductional division varies for different centromere-linked markers (*e.g.*, compare *trp1* and *leu1*, Table 6). This suggests that the frequency of autonomous aberrant or reductional segregation events may be chromosome specific. An interesting question is whether the level or distribution of recombination events on a particular chromosome influences its segregational behavior during the single division of sporulation. Chromosomal variations in recombination behavior might be due to size differences or to constraints imposed by the gene functions located on the chromosome. However, it is important also to consider that the recovery of aberrant segregation products could depend upon the ability of the yeast cell to tolerate aneuploidy for each chromosome (BRUENN and MORTIMER 1971; PERRY and COX 1970).

Hypotheses for the occurrence of an equational division during sporulation: There are at least three hypotheses that can explain the occurrence of a single equational division during sporulation in the majority of *spo12–1* and *spo13–1* cells: (1) replacement of meiosis I and II with a mitotic division, (2) an equational centromere division during meiosis I and subsequent failure of meiosis II, and (3) failure of meiosis I chromosome segregation followed by meiosis II.

Does mitosis replace meiosis I and meiosis II in spo12–1 *and* spo13–1 *strains?* Mutants that may be defective in the regulation of "meiotic *versus* mitotic" functions have been previously described (BAKER *et al.* 1976; GOLUBOVSKAYA 1979). For example, in the ameiotic (*am*) mutant of maize, a single division that cytologically resembles mitosis in most respects, including the absence of pairing and genetic exchange, replaces both meiotic divisions (PALMER 1971). Two lines of evidence from our study argue against the view that *spo12–1* and *spo13–1* undergo an "ameiotic" meiosis. The first is the occurrence of high levels of recombination during sporulation of *spo12–1* and *spo13–1*, indicating that the strains enter meiosis and complete a landmark event of meiotic prophase. Second, the presence of dyads in which a single reductional division takes place indicates that normal events of meiosis I are executed in a fraction of the population.

Does an equational centromere division replace a reductional division during meiosis I, causing failure of meiosis II? The premise of the second hypothesis is that failure of the meiosis II division occurs because chromosomes or unpaired and therefore divide equationally at meiosis I. Some mutations that affect chromosome pairing have been shown to result in the complete failure of one of the two meiotic divisions (JOHNSSON 1944; LEVAN 1940; STRINGHAM 1970). For example, cytological studies of the asynaptic *as* and *as3* mutants of the plant *Brassica campestris* revealed that the unpaired univalents divide equationally at

anaphase I (STRINGHAM 1970). The chromatids fail to segregate at meiosis II, resulting in the formation of diploid or near-diploid products.

While *spo12–1* and *spo13–1* are clearly not asynaptic, since meiotic levels of recombination are observed, they could be defective in maintenance of synapsis after recombination is complete. However, the finding that a small percentage of the dyads undergo a single reductional division makes this hypothesis less tenable. If *spo12–1* and *spo13–1* were leaky alleles and the strains occasionally underwent a reductional meiosis I division, a normal meiosis II should follow, resulting in the production of four haploid spores.

Do spo12–1 *or* spo13–1 *initiate but fail to complete meiosis I and then proceed to meiosis II?* Only a few mutants have been described that fail to complete the meiosis I division and then proceed to meiosis II (LEVAN 1940; SMITH 1939). Mutants of this type may be defective in "signals" regulating the start of meiosis I and/or meiosis II or in an essential component of the meiosis I division apparatus. There are several ways whereby an interruption of meiosis I after completion of recombination could be followed by a meiosis II division: (1) a defective "signal" for movement (congression) of the paired homologs to the meiosis I metaphase plate or for reductional chromosome separation, resulting in a failure of these events and a normal progression to meiosis II, (2) a defective meiosis I spindle apparatus or centromere-spindle attachment site on the paired chromosomes, and (3) a precocious "signal" for the initiation of meiosis II that interrupts and terminates meiosis I. Potentially, the genetic consequences of each would be similar. Desynapsis of the paired homologs would occur, resulting in the presence of univalents at the time of the meiosis II equational division.

This general hypothesis, unlike the previous ones, offers an explanation for the occurrence of some dyads that undergo a single reductional division. If, in a small proportion of the cells, homologs remained paired at the time of congression to the meiosis II metaphase plate, a reductional division might ensue. The presence of paired chromosomes at the time of the meiosis II division could be due to variation in the timing of desynapsis relative to the signal to divide, as a consequence of the disruption of the normal sequence of events of meiosis by *spo12–1* or *spo13–1*. Similarly, aberrant or reductional segregation of some, but not all, chromosomes might reflect asynchrony in the timing of desynapsis of each chromosome.

Cytological evidence in support of the view that cells initiate aspects of meiosis I and then enter and complete meiosis II comes from electron microscope studies of ATCC4117 (MOENS 1974; MOENS *et al.* 1977), the strain from which *spo12–1* and *spo13–1* were isolated (GREWAL and MILLER 1972; KLAPHOLZ and ESPOSITO 1980). MOENS (1974) and MOENS *et al.* (1977) observed that during sporulation of ATCC4117, synaptonemal complexes are present and a meiosis I-like or mitotic spindle is replaced by a more developed spindle with characteristically "modified" meiosis II spindle pole bodies (MOENS and RAPPORT 1971; PETERSON, GRAY and RIS 1972). Cytological studies of *spo12–1* and *spo13–1* are in progress to determine if each behaves like ATCC4117.

In summary, two major conclusions about the interrelationships among landmark events of meiosis in yeast can be drawn from our genetic studies of recombination and segregation in *spo12–1* and *spo13–1* diploids. (1) Equational centromere division during meiosis does not depend upon prior reductional chromosome segregation. (2) Meiotic levels of recombination are not obligatorily associated with reductional division. Equational division of homologs following meiotic levels of exchange has been previously observed in tetrad-producing strains returned from sporulation medium to vegetative growth (ESPOSITO and ESPOSITO 1974). The behavior of *spo12–1* and *spo13–1* raises the intriguing possibility that sporulating cells may "return to vegetative growth" *via* meiosis II.

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Corresponding editor: F. SHERMAN