A MEIOTIC MUTANT AFFECTING RECOMBINATION IN FEMALE *DROSOPHILA MELANOGASTER*[1]

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ABSTRACT

mei-S282 is a female meiotic mutant isolated from a natural population of *Drosophila melanogaster*. It is a recessive mutation located at approximately map position 5 on the third chromosome which has two major effects. It causes a nonuniform decrease in recombination which is most drastic in distal chromosome regions and nondisjunction of all chromosome pairs is elevated at the first meiotic division. Nondisjunctional events are positively correlated; furthermore, nondisjoining chromosomes, themselves nonrecombinant, are preferentially recovered from cells in which nonhomologs are preferentially recovered from cells in which nonhomologs are also non-recombinant.——It is concluded that *mei-S282* is a defect which occurs early in meiosis I prior to the time of exchange. In the mutant, the frequency of no-exchange tetrads for each of the major chromosomes is increased—and in cells which contain two or more no-exchange tetrads, an interaction between these chromosomes leads to correlated nondisjunction. *mei-S282+* then, is an exchange precondition necessary for the normal frequency and distribution of exchanges.

IN higher animals, meiosis is comprised of two successive cell divisions that result in the production of four haploid gametocytes. Although many cytological, genetic, and some biochemical analyses of meiosis have been undertaken in a variety of organisms, a comprehensive understanding of the physiological processes, as well as the time sequence of events involved, is lacking.

A fundamental precept of biology is that all cellular processes are ultimately under genic control; meiosis is no exception. Thus, one way to study the meiotic divisions is to investigate individual genes whose action is necessary for normal meiosis. A number of such meiotic mutants are known in a variety of organisms, and the characterization of the effects of these has led to increased understanding of the meiotic process (for a review of this general subject, see LINDSLEY *et al.* 1968 and NICOLETTI 1968).

SANDLER *et al.* (1968) initiated a systematic search for meiotic mutants from a natural population of *Drosophila melanogaster*. They succeeded in isolating several new meiotic mutants, two of which have been intensively characterized (*mei-S51*, ROBBINS 1971; *mei-S332*, DAVIS 1971). This report presents a genetic analysis of another of their mutants, *mei-S282* .This mutant is a recessive located

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on the third chromosome whose normal allele is required for a normal first meiotic division in females. The mutant has no detectable effect on meiosis in males. Both recombination and chromosome disjunction are altered by *mei-S282*; nondisjunction of all chromosome pairs is elevated and recombination is reduced in a nonuniform manner with the decrease being most pronounced in distal regions. From this investigation, it is concluded that the mutant *mei-S282* alters preconditions for exchange (rather than the exchange event *per se*) in such a way that total recombination is reduced and the spatial distribution of crossovers more closely reflects physical distance than does the distribution in wild-type controls. As a result of this defect, there are increased numbers of meioses in which most or all chromosomes fail to recombine; in such cells, nondisjunction of one or more chromosome pairs may occur. *mei-S282*$^+$, then, is a gene that determines a precondition for exchange that is necessary for the normal frequency and distribution of exchanges.

ISOLATION OF *mei-S282*

mei-S282 was isolated from a natural population by SANDLER *et al.* (1968). Their original stock contained a *2-3* complement (one second and one third chromosome) derived from a single male; these chromosomes were maintained in heterozygous condition with the second chromosome balancer *SM1* and the third chromosome balancer *TM2* (for a description of these chromosomes, see LINDSLEY and GRELL 1968). Flies homozygous for either or both of the autosomes from the *mei-S282 2-3* complement were tested for increased rates of *X* and fourth chromosome nondisjunction and loss at either the first or second meiotic division in females, and increased rates of fourth chromosome nondisjunction and loss at either meiotic division in males (SANDLER *et al.* 1968). It was concluded that *mei-S282* (1) is a complete recessive, (2) is located on the third chromosome, (3) affects the first meiotic division in females (that only the first meiotic division is altered is indicated by the absence of equational exceptional progeny from mutant females), and (4) has no detectable effect in males.

For further testing, stocks were made by the author in which either the second or the third chromosome of the *mei-S282 2-3* complement was replaced by a chromosome derived from Canton-S. The results from crosses in which the tested females were homozygous for the *mei-S282*-derived second chromosome (with Canton-S third chromosomes) or for the *mei-S282*-derived third chromosomes (with Canton-S second chromosomes) indicated that the *mei-S282 2-3* complement also contained a chromosome *2* meiotic mutant. When the behavior of the *X* chromosome was examined in the presence of this mutant, it was found that recombination was increased relative to control values in the region adjacent to the centromere. This second mutant has not been analyzed further. The data of SANDLER *et al.* (1968) on *mei-S282* were obtained in the presence of this mutant; the data to be presented below are from females with Canton-S second chromosomes.

By means of standard mapping procedures using the markers *R Ly H Pr*, *mei-S282* has been located at an approximate position of four units to the right of *R*

in the left arm of chromosome 3. The recombination and disjunctional effects were inseparable. Cytological analysis of all of the salivary gland chromosomes of *mei-S282* has not revealed any detectable aberrations.

RESULTS

RECOMBINATION IN *mei-S282* FEMALES

X chromosome recombination: The effect of *mei-S282* on recombination and nondisjunction was examined in *mei-S282* females having three different sets of *X* chromosome markers. *In(1LR)sc^{v1}, y pn v·y$^+$/y* females and *In(1LR)sc^{v1}, y pn cv m f·y$^+$/y* females were individually mated to *Y^{s}X·Y^L, In(1)EN, v f B/O; C(4)RM, ci ey^R/O* males; *In(1LR)sc^{v1}, y sc cv m f·y$^+$/y* females were individually crossed to *B/Y; C(4)RM, ci ey^R/O* males. The females were homozygous for the fourth chromosome recessive *spa^{pol}*. For all three *X* chromosome constitutions, the third chromosomes of the *mei-S282* females were from the original *mei-S282* genome; those of the control females were from Canton-S. The second chromosomes of the females of the first two *X* constitutions were either homozygous Canton-S or *SM1*/Canton-S. The second chromosomes of the *y sc cv m f·y$^+$/y* females were *b cn c bw*/Canton-S.

The recombination data are given in Table 1. Included in the table are all possible crossover classes and the number of males that appear in each category. The map lengths of each crossover region and of the entire *X* chromosome are also presented. Finally, the number of *X* chromosome exceptions are recorded. With regard to the sex chromosomes, the regular progeny are *B/+* females and *B$^+$* males; the exceptional progeny are *B$^+$* females and *B* males. As a result of an analysis of the *X* chromosome constitution of male progeny of diplo-*X* (*B$^+$*) exceptional females, 44/45 of the exceptional females could be classified as being nonrecombinant (nondisjunction at the first meiotic division); one female was classified as being recombinant (first division). Since the great majority of exceptional progeny contain noncrossover *X* chromosomes, all exceptional progeny have been included as nonrecombinants in the recombination analysis.

In the presence of *mei-S282*, total *X* recombination is reduced relative to that in the control crosses regardless of the second chromosome constitution. The decrease in recombination is greater in distal regions than in the more proximal segments. Considering first the crosses in which both female second chromosomes are uninverted, for the *y sc cv m f·y$^+$* chromosome, the control map length is 62.32 map units. In the presence of *mei-S282* the total *X* map length is about one-third of the control value. In distal to proximal order, the map distances of the four regions in *mei-S282*, as a fraction of the corresponding map distances in the control, are: *sc–cv* (0.28), *cv–m* (0.26), *m–f* (0.41) and *f–y$^+$* (0.60). The same nonuniform reduction in recombination in females homozygous for *mei-S282* is also seen in the crosses involving the other *X* chromosomes.

Structural heterozygosity in one part of the genome in Drosophila usually increases recombination in the remainder of the genome (for a review of the interchromosomal effect, see LUCCHESI and SUZUKI 1968). The inclusion of the

TABLE 1

X *chromosome recombination and disjunctional data*

(1) *In(1LR)sc^{v1}, y pn v·y+/y; spa^{pol}/spa^{pol}* females × *Y^{S} X·Y^{L}, In(1)EN, v f B/0; C(4)RM, ci ey^{R}/0* males
(2) *In(1LR)sc^{v1}, y pn cv m f·y+/y; spa^{pol}/spa^{pol}* females × *Y^{S} X·Y^{L}, In(1)EN, v f B/0; C(4)RM, ci ey^{R}/0* males
(3) *In(1LR)sc^{v1}, y sc cv m f·y+/y; spa^{pol}/spa^{pol}* females × *B/Y; C(4)RM, ci ey^{R}/0* males
(In crosses 1 and 2, maternal second chromosomes are Canton-S; in cross 3 the second chromosomes are Canton-S/*b cn c bw*.)

	y pn^{1}*v^{2}·y+/y				y pn^{1}cv^{2}m^{3}f^{4}·y+/y				y sc^{1}cv^{2}m^{3}f^{4}·y+/y	
	+ + / + +	SM1 + / + +	+ 282 / + 282	SM1 282 / + 282	+ + / + +	SM1 + / + +	+ 282 / + 282	SM1 282 / + 282	+ + / + +	+ 282 / + 282
B/+ ♀ ♀	8432	9273	1401	1037	2387	1916	745	2328	2446	1789
B+ ♀ ♀	0	3	13	29	0	2	6	53	8	33
v f B ♂ ♂	8	14	19	23	0	3	5	63	8	39
Crossover region 0	5411	5228	976	750	1353	940	503	1608	738	928
1	2854	3521	162	150	250	278	44	161	116	29
2	2366	2833	188	170	526	487	101	317	396	86
3	....	....	....	....	311	299	78	219	213	72
4	....	....	....	....	136	153	37	159	83	55
Total single crossover males	5220	6354	350	320	1223	1217	260	856	808	242
1–2	505	1496	8	12	12	29	3	10	13	2
1–3	....	....	....	....	36	80	4	14	20	4
1–4	....	....	....	....	10	63	2	19	17	1
2–3	....	....	....	....	46	64	2	17	23	1
2–4	....	....	....	....	28	56	6	33	29	1
3–4	....	....	....	....	7	6	0	6	6	4

Total double crossover males	505	1496	8	12	139	298	17	99	108	13
1–2–3	....	....	....	....	1	1	0	1	2	0
1–2–4	....	....	....	....	1	6	0	1	1	0
1–3–4	....	....	....	....	0	4	0	3	0	0
2–3–4	....	....	....	....	1	0	2	2	4	2
Total triple crossover males	....	....	....	....	3	11	2	7	7	2
Total quadruple crossover males	....	....	....	....	0	1	0	0	0	0
Total males	11136	13078	1334	1082	2718	2467	782	2570	1661	1185
Map length										
1	30.14	38.31	12.45(.41)†	14.29(.37)‡	11.41	18.69	6.68(.59)	7.78(.42)	10.08	2.86(.28)
2	25.76	33.06	14.35(.56)	16.05(.49)	22.63	26.05	14.38(.64)	14.18(.54)	27.91	7.32(.26)
3	....	....	....	....	14.79	18.41	10.84(.73)	9.75(.53)	15.98	6.60(.41)
4	....	....	....	....	6.73	11.69	5.93(.88)	8.30(.71)	8.35	5.01(.60)
Total map length	55.90	71.37	26.80(.48)	30.34(.43)	55.56	74.84	37.83(.68)	40.01(.53)	62.32	21.79(.35)

* These numbers denote crossover regions.
† These numbers denote *mei-S282* map length relative to the +/+; +/+ control values.
‡ These numbers denote *SM1*/+; *mei-S282*/*mei-S282* map length relative to the *SM1*/+; +/+ control values.

heterozygous *SM1* inversion complex in two of the series of crosses makes it possible to study this phenomenon in the presence of wild-type and *mei-S282* third chromosomes. In the *mei-S282*$^+$ crosses the usual interchromosomal effect obtains. Thus, heterozygosity for *SM1* increases recombination considerably. For the *y pn cv m f-y*$^+$ *X* chromosome, the total map length changes from 55.56 units to 74.84 units, an increase of 35%. Each map interval also increases in length, though the increase is not uniform throughout the chromosome. The distal *pn–cv* and proximal *f–y*$^+$ intervals exhibit increases of 64% and 74% respectively above control values while the middle *cv–m* and *m–f* regions are increased, respectively, to 15% and 25% above control values. In the presence of *mei-S282*, however, second chromosome inversion heterozygosity has a greatly diminished effect on *X* recombination. In the *y pn cv m f-y*$^+$ cross, the *mei-282* map distance of 37.83 is changed to 40.01 units, an increase of only 6%. The distal *pn–cv* and proximal *f–y*$^+$ intervals exhibit increases of 17% and 40%, respectively, above control values while the middle *cv–m* and *m–f* regions are in fact decreased below control values 1% and 10% respectively. Thus, overall, the interchromosomal effect is greatly decreased in *mei-S282* females; possibly only in the proximal *f–y*$^+$ region is an influence of the inversion heterozygosity manifest.

Another way of viewing *X* chromosome recombination data is presented in Figure 1. The relative map positions of markers in *mei-S282* crosses are plotted against the relative positions of the same markers in control crosses. The coordinates of any point represent the map distance of a marker from the left-most marker used in the mutant genotype on the ordinate *versus* the control genotype on the abscissa. Furthermore, the slope of the line between two successive points

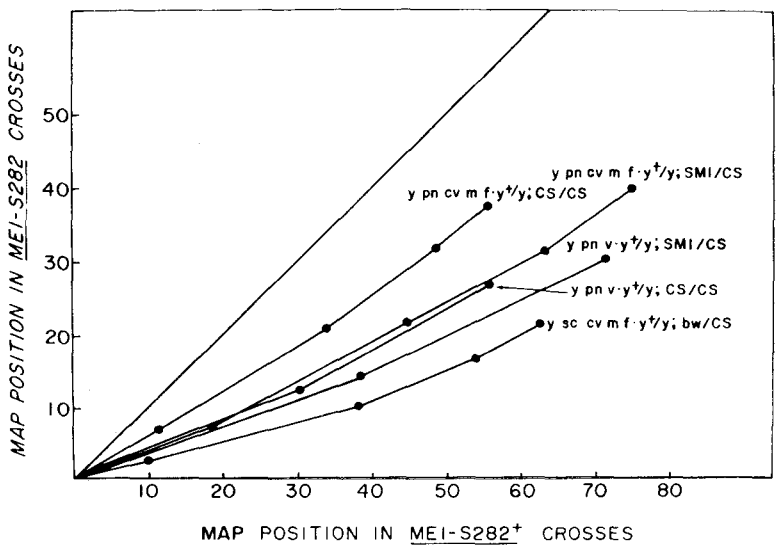

FIGURE 1.—*X* chromosome—cumulative map distance of markers from the most distal marker used in *mei-S282* genotypes on the ordinate plotted against the same distance measured in *mei-S282*+ crosses on the abscissa. The line with slope = 1 expected if the two maps were identical is included as reference.

on any curve represents the distance between successive markers in the mutant genotype relative to the control distance. A slope of 1 indicates identical distance in the two genotypes; the reference line of slope = 1 is included in the figure. In general, the curves in Figure 1 show a constant slope that increases only in the centromere region and the region adjacent to that.

Although the above experiments show considerable variation in total *X* recombination, in all *mei-S282* experiments the altered pattern of recombination remains constant; that is, the reduction in recombination is most pronounced in distal chromosome regions. It is probable that the observed variation is due to the sensitivity of the mutant to both background genotype and unknown environmental conditions.

Second chromosome recombination: Recombination was measured in the right arm of the second chromosome in two separate experiments. In the first experiment, *b cn c bw*/Canton-S females were crossed to *b cn c bw/b cn c bw* males; in the second experiment, *b cn c bw*/Canton-S; spa^{pol}/spa^{pol} females were mated with *B/Y; b cn c bw/b cn c bw; C(4)RM, ci* $ey^R/0$ males. The marker *b* is just to the left of the centromere so that recombination can be followed in the centromere region as well as in the right arm of chromosome *2*.

The recombination data and map distances for each experiment are presented, together with those of the controls, in Table 2. The fourth-chromosome phenotypes of the progeny from cross 2 are not indicated. As is observed for the *X* chromosome, recombination in *mei-S282* females is reduced and the decrease in recombination is most severe in distal chromosome regions. Here, too, variation in recombination frequency in *mei-S282* females is apparent (the total map length in cross 1 is 27.04 units while in cross 2 it is 18.93 units) but, as before, the altered recombination pattern remains the same.

Some of the recombination data for *2*R are presented in Figure 2 which is constructed in the same way as Figure 1, except that the centric region (*b–cn*) is to the left in this figure. This region shows a marked increase in slope in both crosses; the more distal regions show constant slopes. These slope changes are consistent with the nonuniformly altered recombination in *mei-S282*.

Tetrad analyses by the method of WEINSTEIN (1936) have been performed for both the control and *mei-S282 X* and *2*R recombination data (Table 3). For both pairs of chromosomes, *mei-S282* increases the frequency of E_0 tetrads and concomitantly decreases the frequencies of single and multiple exchange tetrads relative to the control. In the presence of the mutant, the distribution of tetrads is virtually the same for a given *X* chromosome constitution regardless of the female second chromosome constitution.

Simultaneous X *and Second Chromosome Recombination:* Since *mei-S282* affects the pattern of recombination on the *X* chromosome and the right arm of chromosome *2* in a similar manner, it is of interest to determine whether recombination occurs independently in each chromosome pair in the mutant genome. In normal meiotic cells, recombination in any chromosome arm occurs independently of recombination events occurring elsewhere in the genome. Nonindependent chromosome behavior in the mutant would be predicted from a class

TABLE 2

Recombination data and map distances for 2R: *(1)* b cn c bw/+ *females* × b cn c bw/b cn c bw *males (male and female progeny) (2)* b cn c bw/+; spa^{pol}/spa^{pol} *females* × B/Y; b cn c bw/b cn c bw; C(4)RM, ci $ey^R/0$ *males (male progeny)*

	Female constitution			
	$b^{3*}cn^2c^1bw/+$			
Crossover region	1 mei-S282+	mei-S282	2 mei-S282+	mei-S282
0	1698	1844	976	1016
1	703	371	403	102
2	384	224	219	69
3	63	62	40	36
Total single crossovers	1150	657	662	217
1–2	39	4	15	5
1–3	22	4	10	4
2–3	12	3	6	3
Total double crossovers	73	11	31	12
1–2–3	0	0	0	1
Total progeny	2921	2512	1669	1236
Map length				
1	26.15	15.09 (.58)†	25.64	9.06 (.35)
2	14.89	9.20 (.62)	14.38	6.31 (.44)
3	3.32	2.75 (.83)	3.36	3.56(1.06)
Total map length	44.36	27.04 (.61)	43.38	18.93 (.44)

* These numbers refer to crossover regions.
† These numbers denote *mei-S282* map length relative to the control values.

of hypotheses describing the action of *mei-S282+* which was consistent with the original *mei-S282* data (SANDLER *et al.* 1968). In one such model, it was postulated that *mei-S282+* is a cellular control signal determining the duration of homologous pairing in meiosis. If pairing is initiated at centromeres and proceeds distally along chromosome arms, premature termination of pairing (the *mei-S282* defect) would result in recombination frequencies which are decreased along the chromosome in the nonuniform manner characteristic of the mutant. If such pairing is synchronous for all tetrads of a meiocyte, precocious termination of pairing in *mei-S282* females should result in meiocytes in which the extent of pairing in one chromosome pair will reflect that of all other tetrads in the same cell. Consequently, the number of ova in which two chromosomes exhibit the same number of crossover events should be much higher than the number expected if the pairing states of the chromosomes were independent.

The question of recombination independence can be critically examined by simultaneously measuring recombination on two nonhomologs. To do this, *In(1LR)sc^{VI}, y sc cv m f y+/y; b cn c bw/+; spa^{pol}/spa^{pol}* females were individually mated to *B/Y; b cn c bw/b cn c bw; C(4)RM, ci ey^R/O* males. Regular

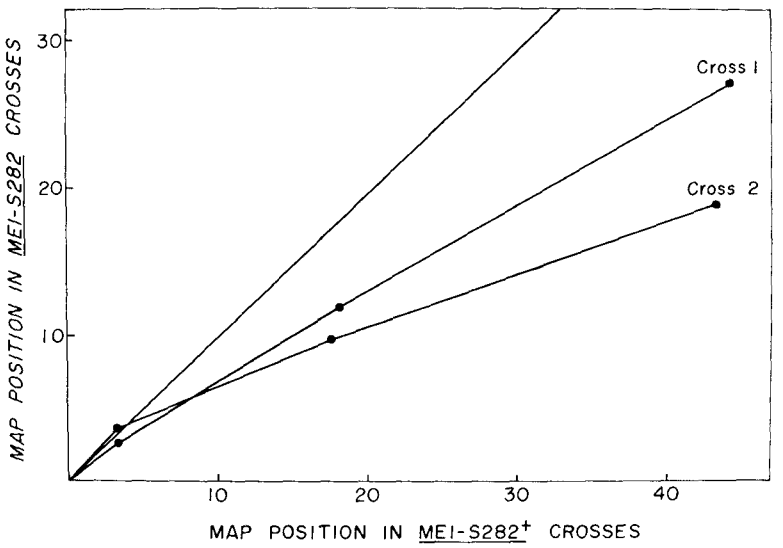

FIGURE 2.—Second chromosome—cumulative map distance of markers on 2R from the leftmost (proximal) marker used in *mei-S282* flies on the ordinate plotted against the same distance measured in *mei-S282+* crosses on the abscissa. The line with slope = 1 expected if the two maps were identical is included as reference. The markers used in both crosses are *b cn c* and *bw*.

X males were scored for recombination on the *X* chromosome and on *2R* and nondisjunction of the fourth chromosomes; *X*-exceptional males were scored for recombination on *2*R and nondisjunction of chromosome *4*. Female progeny were scored only for *X* and fourth chromosome nondisjunction.

Each male phenotype is recorded, together with the total of such offspring, in Table 4 for both the control and *mei-S282* crosses. The phenotypes have been arranged according to the crossover state of the *X* chromosome such that each *X* crossover state is combined with all possible second chromosome crossover constitutions. The separate recombination data are given in Table 1 for the *X* chromosome and in Table 2 for chromosome *2*.

In the presence of *mei-S282*, the *X* map is reduced to 35% of the control value, while the map of *2*R is 44% of its control. The similarity in these two values suggests that the same overall reduction per arm in crossing over is effected in heterologous chromosomes by *mei-S282*.

In these crosses, the recovery of reciprocal noncrossover and crossover classes is unequal for both chromosomes. Such differences are probably due to differential viability of different marker combinations and are to be expected when nine markers are segregating in a cross. In general, the discrepancy is greater in control data.

To determine whether the recombination states of chromosomes within a given meiocyte are independent, a contingency test of the hypothesis of independence was performed for both the control and *mei-S282* data. The *X*-exceptional males which occurred are considered to be noncrossover for the *X* chromosomes and

TABLE 3

Relative frequencies of tetrads of different rank from the X chromosome recombination data (from Table 1) and from the recombination data for the right arm of chromosome 2 (from Table 2)

	Female constitution													
	y pn v·y⁺/y				y pn cv m f·y⁺/y				y sc cv m f·y⁺/y		b cn c bw/+ (1)		b cn c bw/+ (2)	
Exchange rank	+ / + +	SM1 / + +	+ 282 / + 282	SM1 282 / + 282	+ / + +	SM1 / + +	+ 282 / + 282	SM1 282 / + 282	+ / + +	+ 282 / + 282	+ / + +	+ 282 / + 282	+ / + +	+ 282 / + 282
E_0	.06	.03	.49	.44	.11	.01	.34	.36	.03	.61	.21	.47	.21	.67
E_1	.76	.51	.49	.52	.68	.53	.59	.51	.73	.35	.69	.51	.72	.29
E_2	.18	.46	.02	.04	.20	.42	.06	.12	.21	.02	.10	.02	.07	.04
E_3	.00	.00	.00	.00	.01	.04	.02	.02	.03	.01	.00	.00	.00	.00

TABLE 4

Phenotypes of male progeny which appear in the cross of In(1LR)sc^{V1}, y sc cv m f·y+/y; b cn c bw/+; spa^{pol}/spa^{pol} *females* × B/Y; b cn c bw/b cn c bw; C(4)RM, ci ey^{R}/0 *males*

Crossover state		Chromosome genotype		Progeny: Fourth chromosome phenotype From +/+ ♀ (controls)				From *mei-S822/mei-S282* ♀			
X	2	X	2	+	pol	ci	ey^{R}	+	pol	ci	ey^{R}
NCO	NCO	. . . B	+ + + +	3	..	..		19	..	..	
		. . . B	b cn c bw	..	..	..		12	..	..	
		. . . B	+ + + +	..	..	..		..	..	..	5
		. . . B	b cn c bw	..	..	1		..	1	..	
NCO	SCO 1*	. . . B	+ + + bw	1	..	..		..	..	..	
	2	. . . B	+ + c bw	1	..	..		..	..	..	
		. . . B	b cn + +	1	..	..		1	..	..	
	3	. . . B	b + + +	0	..	..		1	..	..	
NCO	DCO 1–3	. . . B	+ cn c +	1	..	..		0	..	..	
NCO	NCO	y + + + +	+ + + +	183	..	..		272	..	..	
		y + + + +	b cn c bw	181	..	..		231	..	..	
		y + + + +	+ + + +	..	..	1		..	4	..	
		y + + + +	b cn c bw	..	..	..		..	3	..	
		y + + + +	b cn c bw	..	..	..		..	..	3	
		+ sc cv m f	+ + + +	50	..	..		200	..	..	
		+ sc cv m f	b cn c bw	19	..	..		44	..	..	
		+ sc cv m f	+ + + +	..	..	..		..	3	..	
		+ sc cv m f	+ + + +	..	..	..		..	..	2	
NCO	SCO 1	y + + + +	+ + + bw	78	..	..		35	..	..	
		y + + + +	b cn c +	61	..	..		16	..	..	
	2	y + + + +	+ + c bw	44	..	..		19	..	..	
		y + + + +	b cn + +	41	..	..		25	..	..	
	3	y + + + +	+ cn c bw	9	..	..		13	..	..	
		y + + + +	b + + +	7	..	..		10	..	..	
	1	+ sc cv m f	+ + + bw	24	..	..		16	..	..	
		+ sc cv m f	b cn c +	9	..	..		7	..	..	
	2	+ sc cv m f	+ + c bw	12	..	..		8	..	..	
		+ sc cv m f	b cn + +	3	..	..		6	..	..	
	3	+ sc cv m f	+ cn c bw	2	..	..		1	..	..	
		+ sc cv m f	b + + +	1	..	..		2	..	..	
NCO	DCO 1–2	y + + + +	+ + c +	1	..	..		3	..	..	
	1–2	y + + + +	b cn + bw	7	..	..		1	..	..	
	1–3	y + + + +	+ cn c +	1	..	..		1	..	..	
	1–3	y + + + +	b + + bw	1	..	..		0	..	..	
	2–3	y + + + +	b + c bw	1	..	..		0	..	..	
	2–3	y + + + +	+ cn + +	1	..	..		0	..	..	
	2–3	+ sc cv m f	+ cn + +	1	..	..		1	..	..	
	2–3	+ sc cv m f	b + c bw	0	..	..		1	..	..	
NCO	TCO 1–2–3	y + + + +	b + c +	0	..	..		1	..	..	
SCO 1	NCO	y sc + + +	+ + + +	28	..	..		14	..	..	

TABLE 4—Continued

Crossover state		Chromosome genotype		Progeny Fourth chromosome phenotype From +/+♀ (controls)				From *mei-S822/mei-S282*♀			
X	2	X	2	+	pol	ci	ey^R	+	pol	ci	ey^R
		y sc + + +	b cn c bw	30	..	..		3	..	..	
		y sc + + +	b cn c bw	..	..	..		..	1	..	
		+ + cv m f	+ + + +	11	..	..		5	..	..	
		+ + cv m f	b cn c bw	3	..	..		1	..	..	
SCO 2	NCO	y sc cv + +	+ + + +	69	..	..		19	..	..	
		y sc cv + +	b cn c bw	42	..	..		14	..	..	
		+ + + m f	+ + + +	65	..	..		34	..	..	
		+ + + m f	b cn c bw	50	..	..		12	..	..	
SCO 3	NCO	y sc cv m +	+ + + +	37	..	..		14	..	..	
		y sc cv m +	b cn c bw	7	..	..		3	..	..	
		+ + + + f	+ + + +	50	..	..		22	..	..	
		+ + + + f	b cn c bw	33	..	..		14	..	..	
SCO 4	NCO	y sc cv m f	+ + + +	9	..	..		10	..	..	
		y sc cv m f	b cn c bw	3	..	..		2	..	..	
		+ + + + +	+ + + +	19	..	..		19	..	..	
		+ + + + +	b cn c bw	16	..	..		18	..	..	
SCO 1	SCO 1	y sc + + +	+ + + bw	11	..	..		1	..	..	
		y sc + + +	b cn c +	7	..	..		0	..	..	
		+ + cv m f	+ + + bw	1	..	..		1	..	..	
		+ + cv m f	b cn c +	1	..	..		0	..	..	
	2	y sc + + +	+ + c bw	8	..	..		0	..	..	
		y sc + + +	b cn + +	6	..	..		0	..	..	
		+ + cv m f	+ + c bw	2	..	..		0	..	..	
		+ + cv m f	b cn + +	0	..	..		1	..	..	
	3	y sc + + +	+ cn c bw	5	..	..		0	..	..	
		y sc + + +	b + + +	1	..	..		1	..	..	
SCO 2	SCO 1	y sc cv + +	+ + + bw	27	..	..		2	..	..	
		y sc cv + +	b cn c +	17	..	..		1	..	..	
		+ + + m f	+ + + bw	33	..	..		1	..	..	
		+ + + m f	b cn c +	20	..	..		2	..	..	
	2	y sc cv + +	+ + c bw	10	..	..		0	..	..	
		y sc cv + +	b cn + +	10	..	..		1	..	..	
		+ + + m f	+ + c bw	20	..	..		0	..	..	
		+ + + m f	b cn + +	14	..	..		0	..	..	
	3	y sc cv + +	+ cn c bw	3	..	..		0	..	..	
		y sc cv + +	b + + +	1	..	..		0	..	..	
		+ + + m f	+ cn c bw	1	..	..		0	..	..	
		+ + + m f	b + + +	6	..	..		0	..	..	
SCO 3	SCO 1	y sc cv m +	+ + + bw	14	..	..		2	..	..	
		y sc cv m +	b cn c +	7	..	..		0	..	..	
		+ + + + f	+ + + bw	23	..	..		5	..	..	
		+ + + + f	b cn c +	19	..	..		4	..	..	
	2	y sc cv m +	+ + c bw	2	..	..		1	..	..	
		y sc cv m +	b cn + +	3	..	..		0	..	..	
		+ + + + f	+ + c bw	7	..	..		0	..	..	
		+ + + + f	b cn + +	5	..	..		2	..	..	
	3	y sc cv m +	+ cn c bw	2	..	..		0	..	..	

TABLE 4—Continued

Crossover state		Chromosome genotype		Progeny Fourth chromosome phenotype From +/+ ♀ (controls)				From *mei-S822/mei-S282* ♀			
X	2	X	2	+	pol	ci	ey^R	+	pol	ci	ey^R
		y sc cv m +	b + + +	0	..	..		1	..	..	
		+ + + + f	+ cn c bw	0	..	..		1	..	..	
		+ + + + f	b + + +	0	..	..		1	..	..	
SCO 4	SCO 1	y sc cv m f	+ + + bw	6	..	..		1	..	..	
		y sc cv m f	b cn c +	0	..	..		1	..	..	
		+ + + + +	+ + + bw	11	..	..		2	..	..	
		+ + + + +	b cn c +	5	..	..		2	..	..	
	2	y sc cv m f	+ + c bw	1	..	..		1	..	..	
		y sc cv m f	b cn + +	1	..	..		1	..	..	
		+ + + + +	+ + c bw	7	..	..		0	..	..	
		+ + + + +	b cn + +	2	..	..		2	..	..	
	3	y sc cv m f	b + + +	0	..	..		2	..	..	
		+ + + + +	b + + +	0	..	..		1	..	..	
		+ + + + +	+ cn c bw	1	..	..		1	..	..	
SCO 1	DCO 1–2	y sc + + +	+ + c +	2	..	..		0	..	..	
		+ + cv m f	+ + c +	0	..	..		1	..	..	
SCO 2	DCO 1–2	+ + + m f	+ + c +	2	..	..		0	..	..	
	1–3	y sc cv + +	b + + bw	1	..	..		0	..	..	
		y sc cv + +	+ cn c +	2	..	..		0	..	..	
		+ + + m f	b + + bw	1	..	..		0	..	..	
	2–3	+ + + m f	+ cn + +	1	..	..		0	..	..	
		+ + + m f	b + c bw	1	..	..		0	..	..	
SCO 3	DCO 1–2	+ + + + f	+ + c +	1	..	..		0	..	..	
	1–3	y sc cv m +	+ cn c +	1	..	..		1	..	..	
		+ + + + f	+ cn c +	1	..	..		1	..	..	
	2–3	+ + + + f	+ cn + +	1	..	..		0	..	..	
SCO 4	DCO 1–2	+ + + + +	b cn + bw	1	..	..		0	..	..	
	1–3	+ + + + +	+ cn c +	1	..	..		1	..	..	
	2–3	+ + + + +	b + c bw	0	..	..		1	..	..	
DCO 1–2	NCO	y + cv + +	+ + + +	0	..	..		1	..	..	
		+ sc + m f	+ + + +	6	..	..		1	..	..	
		+ sc + m f	b cn c bw	2	..	..		2	..	..	
DCO 1–3	NCO	y + cv m +	+ + + +	1	..	..		0	..	..	
		y + cv m +	b cn c bw	2	..	..		0	..	..	
		+ sc + + f	+ + + +	4	..	..		0	..	..	
		+ sc + + f	b cn c bw	8	..	..		0	..	..	
DCO 1–4	NCO	y + cv m f	+ + + +	1	..	..		0	..	..	
		y + cv m f	b cn c bw	0	..	..		1	..	..	
		+ sc + + +	+ + + +	3	..	..		0	..	..	
		+ sc + + +	b cn c bw	3	..	..		0	..	..	
DCO 2–3	NCO	y + + m +	+ + + +	7	..	..		1	..	..	
		y + + m +	b cn c bw	3	..	..		0	..	..	
		+ sc cv + f	+ + + +	2	..	..		0	..	..	
		+ sc cv + f	b cn c bw	1	..	..		0	..	..	
DCO 2–4	NCO	y + + m f	+ + + +	7	..	..		0	..	..	
		+ sc cv + +	+ + + +	9	..	..		0	..	..	

TABLE 4—Continued

Crossover state		Chromosome genotype		Progeny: Fourth chromosome phenotype From +/+ ♀ (controls)				Progeny: Fourth chromosome phenotype From *mei-S822/mei-S282* ♀			
X	2	X	2	+	pol	ci	ey^R	+	pol	ci	ey^R
		+ sc cv + +	b cn c bw	1	..	..		1	..	..	
DCO 3–4 NCO		y + + + f	b cn c bw	1	..	..		0	..	..	
		+ sc cv m +	+ + + +	0	..	..		2	..	..	
		+ sc cv m +	b cn c bw	0	..	..		1	..	..	
DCO 1–2 SCO 1		y + cv + +	+ + + bw	0	..	..		1	..	..	
		+ sc + m f	+ + + bw	1	..	..		0	..	..	
		+ sc + m f	b cn c +	2	..	..		0	..	..	
	2	+ sc + m f	+ + c bw	2	..	..		0	..	..	
DCO 1–3 SCO 1		y + cv m +	+ + + bw	1	..	..		0	..	..	
		y + cv m +	b cn c +	1	..	..		0	..	..	
		+ sc + + f	b cn c +	1	..	..		1	..	..	
	2	+ sc + + f	b cn + +	1	..	..		0	..	..	
	3	+ sc + + f	+ cn c bw	1	..	..		0	..	..	
DCO 1–4 SCO 1		+ sc + + +	+ + + bw	4	..	..		0	..	..	
		+ sc + + +	b cn c +	1	..	..		0	..	..	
		+ sc + + +	+ + + bw	..	..	..	1	0	..	..	
	2	y + cv m f	+ + c bw	1	..	..		0	..	..	
		+ sc + + +	+ + c bw	2	..	..		0	..	..	
DCO 2–3 SCO 1		y + + m +	+ + + bw	2	..	..		0	..	..	
		y + + m +	b cn c +	2	..	..		0	..	..	
		+ sc cv + f	+ + + bw	1	..	..		0	..	..	
		+ sc cv + f	b cn c +	1	..	..		0	..	..	
	2	y + + m +	+ + c bw	2	..	..		0	..	..	
		y + + m +	b cn + +	1	..	..		0	..	..	
		+ sc cv + f	+ + c bw	1	..	..		0	..	..	
DCO 2–4 SCO 1		y + + m f	+ + + bw	3	..	..		0	..	..	
		+ sc cv + +	+ + + bw	2	..	..		0	..	..	
	2	y + + m f	+ + c bw	2	..	..		0	..	..	
		y + + m f	b cn + +	2	..	..		0	..	..	
		+ sc cv + +	+ + c bw	3	..	..		0	..	..	
DCO 3–4 SCO 1		y + + + f	+ + + bw	2	..	..		0	..	..	
		y + + + f	b cn c +	1	..	..		0	..	..	
	2	y + + + f	+ + c bw	1	..	..		0	..	..	
		y + + + f	b cn + +	1	..	..		0	..	..	
		+ sc cv m +	b cn + +	0	..	..		1	..	..	
DCO 1–4 DCO 1–2		y + cv m f	+ + c +	1	..	..		0	..	..	
TCO 1–2–3 NCO		y sc + m +	+ + + +	1	..	..		0	..	..	
TCO 1–2–4 NCO		+ + cv + +	+ + + +	1	..	..		0	..	..	
TCO 2–3–4 NCO		+ + + m +	+ + + +	2	..	..		0	..	..	
		+ + + m +	b cn c bw	1	..	..		1	..	..	
TCO 1–2–3 SCO 1		y sc + m +	+ + + bw	1	..	..		0	..	..	
2–3–4 SCO 1		+ + + m +	+ + + bw	1	..	..		1	..	..	
Total males				1666	0	3		1212	12	10	

* Abbreviations of crossover states are used as follows: for example, NCO designates a non-crossover chromosome, SCO 1 designates a chromosome which has a single crossover in region 1, etc.

were included as such in the analysis. The data were arranged in a 4×3 contingency table for the control cross and in a 4×4 contingency table for the *mei-S282* cross. The marginals were respectively the various crossover states of the *X* chromosome by the array of crossover states of *2*R. There is one fewer marginal class in the control cross than in *mei-S282* because no second chromosome triple crossovers were recovered from this cross.

In calculating χ^2, classes with expectations less than 1 have been combined to ensure that the smallest expectations considered is at least 1. The number of classes is determined after the combinations have been made (SNEDECOR and COCHRAN 1967). Thus, for the *mei-S282* data, 7 classes have been combined; therefore, the total number of classes is 10 and the degrees of freedom = (number of classes) − (number of estimated parameters) − 1 = 10−6−1 = 3.

The data agree with the null hypothesis that recombination on *2*R occurs independently of that on the *X* chromosome; the *p* value is considerably above the 0.05 level of significance in both experimental and control crosses. For the control, *p* is greater than 0.9 ($\chi^2 = 1.42$ with 5 degrees of freedom); for *mei-S282*, *p* is approximately 0.25 ($\chi^2 = 4.13$ with 3 degrees of freedom). From these data, it is concluded that recombination on the *X* and second chromosomes and—by inference—on all chromosomes is independent in *mei-S282*.

DISJUNCTION IN *mei-S282* FEMALES

The influence of *mei-S282* on disjunction of the *X* and fourth chromosomes was examined in the three crosses described previously. The $Y^sX{\cdot}Y^L$, *In(1)EN*, *v f B/0*; *C(4)RM*, *ci ey*^{R}*/0* males produce four types of sperm: (1) $Y^sX{\cdot}Y^L$; *C(4)RM*, (2) $Y^sX{\cdot}Y^L$; *0*, (3) *0*; *C(4)RM* and (4) *0;0*. The *B/Y*; *C(4)RM*; *ci ey*^{R}*/0* males also produce four sperm types: (1) *X*; *C(4)RM*, (2) *X*; *0*, (3) *Y*; *C(4)RM* and (4) *Y*; *0*. Evidence obtained by DAVIS (1971) indicates that the four sperm classes appear approximately equally frequently; this equality will be assumed in the analyses that follow.

The *X* chromosome segregation classes which appear among the progeny of these matings were included in Table 1. The progeny recorded in Table 1 have been classified according to their *X* and chromosome *4* ova constitution and these data are presented in Table 5. While the total frequency of nondisjunction varies from experiment to experiment, the pattern of exceptional types is roughly the same in the different crosses (e.g., the ratio of *XX;4* to *0;4* ova is constant). Consequently, disjunctional data from the three *mei-S282* experiments are pooled in Table 5. This has also been done for the control crosses and for the analogous *SM1*/Canton-S experiments. In these crosses, *X*-chromosome exceptions are zygotically recoverable only half as frequently as *X*-chromosome regular ova. However, fourth chromosome exceptional and regular zygotes are recovered approximately equally frequently. In order to make the rates of *X*- and fourth-chromosome nondisjunction directly comparable, the number of *X*-exceptional progeny has been doubled to calculate the frequencies in Table 5 which are presented as exceptions/10^3 ova.

Nondisjunction is fairly frequent in *mei-S282* females. Among progeny of

TABLE 5

X *and fourth chromosome disjunctional data from* In(1LR)sc^{v1}, y pn v·y+/y; spa^{pol}/spa^{pol} *females and* In(1LR)sc^{v1}, y pn cv m f·y+/y; spa^{pol}/spa^{pol} *females crossed to* Y^{s}X·Y^{L}, In(1)EN, v f B/0; C(4)RM, ci ey^{R}/0 *males and* In(1LR)sc^{v1}, y sc cv m f·y+/y; spa^{pol}/spa^{pol} *females crossed to* B/Y; C(4)RM, ci ey^{R}/0 *males. The second chromosomes of the females are either homozygous Canton-S,* b cn c bw/*Canton-S or* SM1/*Canton-S*

Female second chromosome constitution		Female third chromosome constitution: +/+				Exceptions 10^3 ova		Female third chromosome constitution: mei-S282/mei-S282				Exceptions 10^3 ova	
		4	44	0	Σ	X	4	4	44	0	Σ	X	4
+/+	X: X ♀	13261	2	2	13265	1.67	.6†	3895	18	22	3935	30.80	12.46
	X: X noncrossover ♂	7500	0	2	7502			2379	15	13	2407		
	X: X crossover ♂	8009	0	4	8013			893	1	0	894		
or		28770 (28766.01)*	2 (3.00)	8 (10.99)	28780			7167 (7156.26)	34 (37.41)	35 (42.33)	7246		
	XX	7 (8.00)	0 (0.00)	1 (0.00)	8			49 (51.43)	2 (0.27)	1 (0.30)	52		
b cn c bw/+	0	13 (15.99)	1 (0.00)	2 (0.01)	16			54 (62.30)	2 (0.33)	7 (0.37)	63		
	Σ	28790	3	11	28804			7270	38	43	7351		
	X: X ♀	11181	1	7	11189	1.57	.9	3316	18	31	3365	44.67	23.80
	X: X noncrossover ♂	6158	5	5	6168			2324	14	20	2358		
	X: X crossover ♂	9377	0	0	9377			1290	3	1	1294		
SM1/+		26716 (26712.02)	6 (8.99)	12 (12.99)	26734			6930 (6887.11)	35 (48.83)	52 (81.06)	7017		
	XX	3 (5.00)	1 (0.00)	1 (0.00)	5			61 (80.48)	6 (0.57)	15 (0.95)	82		
	0	15 (16.99)	2 (0.00)	0 (0.01)	17			61 (84.41)	9 (0.60)	16 (0.99)	86		
	Σ	26734	9	13	26756			7052	50	83	7185		

* These values are expected on the hypothesis that *X* chromosomes and fourth chromosomes nondisjoin independently.

† Haplo-*4* progeny were not included in these tabulations. Tetra-*4* progeny have been assumed to be lethal. Even if they do have an appreciable survival (GRELL 1961) and are phenotypically indistinguishable from regular progeny, this would result in only a small increase in the real rate of fourth chromosome nondisjunction and a decrease in the expected number of *X-4* double exceptions. Thus, any survival of tetra-*4*'s leads to a greater discrepancy between the numbers of expected and observed *X-4* double exceptions.

females lacking the *SM1* inversion, *X*- and fourth-chromosome nondisjunction is 18- to 20-fold higher than in the controls. The addition of the heterozygous inversion to the *mei-S282* genome increases nondisjunction 26 to 28 times control values. Chromosome loss, as inferred from an excess of nullo-exceptions for a given chromosome compared to the diplo-exceptions for the same chromosome, is not very great. In the absence of the *SM1* inversion, the ratios of nullo- to diplo-zygotes for the *X* chromosome (63:52) and chromosome *4* (43:38) do not differ significantly from 1:1. This is true also for the *X* chromosome data from the *SM1* crosses (86:82) but an excess of nullo-zygotes to diplo-zygotes is observed for the fourth chromosome (83:50); thus there is some fourth chromosome loss in *mei-S282* under these circumstances.

Nondisjunction of the *X*- and fourth-chromosome pairs is positively correlated in *mei-S282*. Thus, in the crosses lacking *SM1*, 12 *X* chromosome-fourth chromosome double exceptions were observed, whereas only 1.4 are expected on the assumption of independence. Similarly, among the progeny of *SM1*/Canton-S; *mei-S282/mei-S282* females, 46 double exceptions were recovered when only 3 are expected. Among the double exceptions in all *mei-S282* crosses the proportions of the four classes are approximately those expected if the *X* chromosomes and fourth chromosomes were segregating independently in cells in which they were simultaneously nondisjoining; thus, there is no excess of the nullo-*X*;diplo-*4* and diplo-*X*;nullo-*4* classes relative to the numbers observed for the other two double exceptional classes. An excess of these types would be expected if nonhomologous segregation of the *X* and fourth chromosomes were occurring.

An examination of the control data obtained both in the presence and absence of inversion heterozygosity indicates that here, too, nondisjunction of the *X* and fourth chromosomes is positively correlated. This excess of double exceptions is also consistently detected in other appropriately marked control crosses; in explanation, it has been suggested that such nondisjunction occurs only in a few meiotic cells in which the disruption of a general cellular process affects, with a high probability, more than one chromosome pair (HALL 1970).

The positive correlation in nondisjunction observed in *mei-S282* does not, however, come about because the *X* chromosome and the fourth chromosome are nondisjoining independently in a small fraction of cells in which meiosis goes awry such that the *X* and fourth chromosomes always move to the poles at random at anaphase I. If this were the case, the frequency of ova nondisjunctional for the *X* chromosome and the frequency of ova nondisjunctional for chromosome *4* should be equal. This is not observed in *mei-S282*; the gametic frequency of *X* chromosome nondisjunction is twice that of the fourth chromosome, whether or not *SM1* is present (Table 5). Furthermore, if the chromosomes were assorting randomly within a given cell, then among ova nondisjunctional for the *X* chromosomes the fourth chromosome constitution should be *44:4:0* in the ratio of 1:2:1. From the crosses without *SM1*, among *X*-chromosome exceptional ova the chromosome *4* classes appear in the ratio of 8:206:16; in the presence of *SM1*, the classes are 30:244:62. Similarly, as a result of random segregation, ova nondisjunctional for chromosome *4* should have an X constitution *XX:X:0* in the

ratio of 1:2:1. Without *SM1*, among ova nondisjunctional for chromosome *4* the *X* chromosome classes are 6:69:18; in the *SM1* crosses the classes are 42:87:50. Overall (with the last ratio being the exception) the data are not consistent with *X* and fourth chromosome nondisjunction resulting from a single subset of *mei-S282* meiocytes in which random movement of these chromosomes occurs.

Nondisjunction of the major autosomes is also elevated by *mei-S282*. The effect of the mutant on disjunction of the third chromosomes was examined in mass matings of homozygous *mei-S282* females to attached-third-chromosome-bearing males (SANDLER *et al.* 1968). In such a cross, progeny are produced only when a gamete disomic for the third chromosome from one parent unites with the complementary nullosomic third-chromosome gamete from the other parent. Since no regular ova are recovered, it is possible to detect the occurrence of autosomal nondisjunction but not its absolute frequency. In the experiment of SANDLER *et al.*, there were 435 *X* chromosome exceptions per 10^3 ova among ova nondisjunctional for the third chromosomes (the numbers of *X*-exceptional progeny recorded in SANDLER's table have been doubled to calculate frequencies of gametic nondisjunction), whereas among ova regular for the second and third chromosomes there are 30.8 *X* chromosome exceptions per 10^3 ova (Table 5). Hence nondisjunction of the *X* and third chromosomes is positively correlated. The distribution of *X* chromosome excpetions among diplo-*3* ova (8 *XX*:12 *X*:10 *0*) and among nullo-*3* ova (2 *XX*:14 *X*:0 *0*) is inconsistent with the 1:2:1 ratio expected if the *X* chromosomes were assorting randomly to the anaphase I poles in all of these meioses. The *X* and third chromosomes do not appear to be nondisjoining as a result of nonhomologous segregations. However, the small number of exceptions involved and the fact that the data were obtained with the original *mei-S282* stock which carried an additional second chromosome meiotic mutant would suggest that these results be accepted with caution.

Finally, we may note a relationship between recombination and nondisjunction in *mei-S282* females. It is clear that nondisjunctional events are positively correlated; that is, a meiotic cell in which one pair of chromosomes has nondisjoined has an increased probability of being nondisjunctional for other chromosome pairs. Furthermore, progeny that are exceptional for the fourth chromosomes are almost exclusively nonrecombinant for the *X* or second chromosomes and, similarly, zygotes in which the *X* chromosomes have nondisjoined are nonrandomly nonrecombinant for chromosome *2* (Tables 6, 7). Thus, in the absence of *SM1*, 40 progeny nondisjunctional for chromosome *4* were recovered among 2522 offspring in which the *X* chromosomes were nonrecombinant, whereas only one fourth chromosome exception appeared among 894 progeny in which the *X* chromosomes had recombined. There is, therefore, approximately a ten-fold increase in the recovery of fourth chromosome exceptions among noncrossover *X*-chromosome zygotes. This increase is also observed in crosses in which *SM1* is present. Moreover, progeny exceptional for either the *X* or fourth chromosomes are nonrandomly recovered in ova with noncrossover second chromosomes (Table 7). In fact, in the one cross in which the *X*, second and fourth chromoconstitutions could be simultaneously determined, progeny exceptional for the

TABLE 6

The crossover state of X chromosomes in zygotes which are exceptional for the fourth chromosomes

Female genotype	X chromosomes		Fourth chromosome exceptions	Exceptions/ 10^3 zygotes
+/+; mei-S282+/mei-S282+	NCO	7526	6	0.8
	CO	8013	4	0.5
+/+; mei-S282/mei-S282	NCO	2522	40	15.9
	CO	894	1	1.1
SM1/+; mei-S282+/mei-S282+	NCO	6190	14	2.2
	CO	9377	0	—
SM1/+; mei-S282/mei-S282	NCO	2526	80	31.0
	CO	1294	4	3.1

fourth chromosomes are preferentially nonrecombinant for both the *X* and second chromosomes. In the control crosses, the frequency of progeny exceptional for a particular chromosome is not consistently correlated with the recombination state of the other chromosomes.

DISCUSSION

mei-S282 is a female meiotic mutant in *Drosophila melanogaster* that affects the phenomena of recombination and chromosome disjunction. Recombination is reduced nonuniformly by the mutant; the decreases are most severe in distal chromosome regions and are less pronounced proximally. Nondisjunction of all chromosome pairs is increased at the first meiotic division and nondisjunction of heterologous chromosome pairs is positively correlated. Chromosomes that have nondisjoined are almost all nonrecombinant. Moreover, nondisjoining chromosomes are preferentially recovered from cells in which heterologs are also nonrecombinant.

The nonuniform reduction in recombination which is characteristic of *mei-*

TABLE 7

The crossover state of second chromosomes in zygotes which are exceptional for the X chromosome or chromosome 4

Female genotype	Chromosome 2		X chromosome exceptions	X chromosome exceptions/ 10^3 zygotes	Fourth chromosome exceptions	Fourth chromosome exceptions/ 10^3 zygotes
b cn c bw/+; mei-S282+/mei-S282+	NCO	976	4	4.1	2	2.0
	CO	693	4	5.8	1	1.4
b cn c bw/+; mei-S282/mei-S282	NCO	1015	37	36.5	22*	21.7
	CO	219	2	9.1	0	—

* Of these twenty-two fourth chromosome exceptional progeny, twenty-one are nonrecombinant for the *X* chromosomes.

S282 is also observed, and to a similar degree, among progeny of crosses in which *mei-S282* females are heterozygous for the *SM1* inversion complex. In *mei-S282*$^+$ females, heterozygosity for *SM1* results in the characteristic interchromosomal effect. That recombination is reduced by *mei-S282* and that the increased exchange normally induced by structural heterozygosity is prevented by the mutant suggests that the normal function of *mei-S282*$^+$ occurs prior to or at the time of exchange.

In accord with the earlier ideas of BRIDGES (1915), SANDLER *et al.* (1968) have argued that it should be possible to distinguish between alterations in pre-conditions for exchange (such as pairing) and changes in the frequency of the exchange event itself. Thus, they have suggested that mutants defective in preconditions for exchange would show altered interference, whereas, in those defective in the exchange process, interference should be unchanged. Since the data are very few, per region comparisons of coincidence values between *mei-S282* and the control are not informative. If, however, the regional coincidence values are summed for a given *X* or second chromosome constitution and the average determined, in all instances interference is altered by *mei-S282* (e.g. for the *y sc cv m f·y*$^+$ *X* chromosome, the average coincidence value in the control is 0.57, in *mei-S282* it is 0.90). It is therefore concluded that *mei-S282* is defective in a precondition for exchange. *mei-S282*$^+$, then, is an exchange precondition necessary for the normal frequency and distribution of exchanges.

One way of viewing the interaction between *SM1* and *mei-S282* which is compatible with this description of *mei-S282*$^+$ is the following: in cells in which *mei-S282* is present, the total amount of recombination which can occur is limited and the exchange distribution is nonrandom in that recombination preferentially occurs near the centromere, at the expense of recombination in distal regions. In such cells, heterozygosity for *SM1* increases total recombination only slightly; its major influence is to increase the number of exchanges which have occurred adjacent to the centromere, thereby augmenting the similar action of *mei-S282*, as well as distally, supplementing the *mei-S282*-exchange deficiency in such regions.

That nondisjunction in *mei-S282* occurs only at the first meiotic division is compatible with this as the proposed time of action of the mutant. Recombination occurs independently in the *X* and second chromosomes in *mei-S282* females; this implies that all rather than a subset of meiocytes must be affected by the altered exchange precondition. This is not so with respect to nondisjunction. In *mei-S282* females there is a positive correlation of nondisjunction for all examined pairs of heterologs, which indicates that nondisjunction occurs preferentially in a subset of meiocytes. A question that arises, therefore, is whether the altered patterns of recombination and chromosome disjunction which occur in *mei-S282* can both be attributed to a single defect in an exchange precondition or whether they represent two separate mutant effects.

This question can be resolved by several observations which are compatible with the decreased exchange and increased nondisjunction resulting from one lesion that occurs early in meiosis I. Tetrad analyses indicate that *mei-S282*

increases the frequency of no-exchange tetrads and concomitantly decreases the frequencies of single-and multiple-exchange tetrads relative to the control (e.g. for both the *X* and second chromosomes, the frequency of no-exchange tetrads is approximately 50%). Furthermore, in *mei-S282*, the chromosomes which have nondisjoined are themselves nonrecombinant, suggesting that they are derived from E_0 tetrads. That the frequency of E_0 tetrads greatly exceeds the frequency of nondisjunction (e.g. 3% for the *X* chromosomes) implies that nondisjunction occurs in only a fraction of meiocytes which contain E_0 tetrads. The additional observation that nondisjoining chromosomes are preferentially recovered from cells in which heterologs are nonrecombinant suggests that the meiocytes in which nondisjunction occurs are those which contain more than one E_0 tetrad. The pattern of nondisjunction observed in *mei-S282* suggests that in such cells, the chromosomes do not *all* move to the poles at random. Presumably, an interaction occurs between the E_0 tetrads which leads, at least some of the time, to their correlated nondisjunction. Although the *mei-S282* data on *X* and third chromosome nondisjunction do not indicate that nonhomologous segregations are occurring in such cells, the presence of a second meiotic mutant in the tested stock renders this observation inconclusive.

Under this view, the effects of *mei-S282* on recombination and chromosome disjunction can be attributed to a single defect which occurs prior to the time of exchange in meiosis I. In the mutant, the frequency of no-exchange tetrads for each major chromosome is increased and in cells in which two or more tetrads are simultaneously E_0, an interaction between these chromosomes leads to correlated nondisjunction. Since, normally, fourth chromosomes are always nonrecombinant, one might not expect their disjunction to be affected by a mutant in an exchange precondition. Presumably the meiotic disturbance in *mei-S282* is sufficiently severe to interfere in some way with the normal distributive pairing of fourth chromosomes (GRELL 1964) such that they also nondisjoin in some fraction of meiocytes. Nondisjunction of the *X* and fourth chromosomes is increased slightly above the *mei-S282* values in the presence of *SM1*. Since the frequency of E_0 tetrads for the *X* chromosome is approximately the same in both types of crosses (e.g. 50%) the increased nondisjunction probably results from the elevated frequency of E_0 second chromosomes in *SM1* heterozygotes which are available to interact with other E_0 tetrads.

Recently BAKER and CARPENTER (1972) isolated several *X*-linked meiotic mutants whose behavior is consistent with their being defective in a precondition for exchange. In each of these mutants (1) there is a nonuniform reduction in recombination which is most drastic in distal regions, (2) interference values for noncentromere-spanning regions are different from the control values, and (3) first division nondisjunction is increased for all chromosome pairs. At least some of the nondisjunction is attributed to increases in the no-exchange tetrads and thus to the increased probability of distributive disjunction. From the preceding discussion, it is probable that *mei-S282* is an autosomal representative of this class of meiotic mutants.

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LITERATURE CITED

BAKER, B. and A. T. C. CARPENTER, 1972 Genetic analysis of sex chromosomal meiotic mutants in *Drosophila melanogaster*. Genetics **71**: 255–286.

BRIDGES, C. B., 1915 A linkage variation in Drosophila. J. Expt. Zool. **19**: 1–21.

DAVIS, B. K., 1971 Genetic analysis of a meiotic mutant resulting in precocious sister-centromere separation in *Drosophila melanogaster*. Molec. Gen. Genet. **113**: 251–272.

GRELL, E. H., 1961 The tetrasomic for chromosome *4* in *Drosophila melanogaster*. Genetics **46**: 1177–1183.

GRELL, R. F., 1964 Distributive pairing: the size-dependent mechanism for regular segregation of the fourth chromosome in *Drosophila melanogaster*. Proc. Nat. Acad. Sci. U.S. **52**: 226–232.

HALL, J. C., 1970 Non-independence of primary non-disjunction for the sex and fourth chromosomes in *D. melanogaster*. D. I. S. **45**: 160.

LINDSLEY, D. L. and E. H. GRELL, 1968 Genetic variation of *Drosophila melanogaster*. Carnegie Inst. Wash. Publ. 627.

LINDSLEY, D. L., L. SANDLER, B. NICOLETTI and G. TRIPPA, 1968 Genetic control of recombination in Drosophila. Pp. 253–276. In: *Replication and Recombination of Genetic Material.* Edited by W. J. PEACOCK and R. D. BROCK. Australian Academy of Science, Canberra.

LUCCHESI, J. C. and D. T. SUZUKI, 1968 The interchromosomal control of recombination. Ann. Rev. of Genetics **2**: 53–86.

NICOLETTI, B., 1968 Il controllo genetico della meosi. Atti. Assoc. Genet. Ital. **13**: 1–71.

ROBBINS, L. R., 1971 Nonexchange alignment: a meiotic process revealed by a synthetic mutant of *Drosophila melanogaster*. Molec. Gen. Genet. **110**: 144–166.

SANDLER, L., D. L. LINDSLEY, B. NICOLETTI and G. TRIPPA, 1968 Mutants affecting meiosis in natural populations of *Drosophila melanogaster*. Genetics **60**: 525–558.

SNEDECOR, G. W. and W. G. COCHRAN, 1967 *Statistical Methods*. Pp. 235–236. The Iowa State University Press. Ames, Iowa.

WEINSTEIN, A., 1936 The theory of multiple-strand crossing over. Genetics **21**: 155–199.