APPLICATION OF THE "DISTRIBUTIVE PAIRING" HYPOTHESIS TO PROBLEMS OF SEGREGATION IN TRANSLOCATION HETEROZYGOTES OF *DROSOPHILA MELANOGASTER*¹

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THE distributive pairing hypothesis of GRELL (1962) aims to elucidate the mechanisms involved in chromosome pairing, exchange, and disjunction at meiosis in the female of *Drosophila melanogaster*. It provides a new interpretation of meiosis which can account for many of the seemingly contradictory reports on chromosome behaviour made by earlier authors.

Former ideas on the nature of pairing and disjunction were based largely on the hypothesis of DARLINGTON (1929, 1937). He postulated that chiasmata, formed at points where crossing over had occurred, were responsible for holding bivalents together at meiotic metaphase and ensuring orderly disjunction at anaphase I. However, DOBZHANSKY (1932, 1933) was quick to point out that the example of the *Drosophila* male showed clearly that orderly disjunction could take place even in the complete absence of crossing over. Since then, COOPER (1944, 1945) has drawn attention to a wide variety of species in which regular segregation can occur in chromosomes devoid of chiasmata.

DOBZHANSKY (1931, 1932) put forward the alternative hypothesis of "competitive pairing." He concluded that crossing over did not determine regular disjunction, but believed that both crossing over and disjunction were determined by a "third factor"—namely the intimacy of pairing of homologous chromosomes prior to crossing over. If this pairing were disrupted, e.g., by translocation, inversion, or duplication, the frequency of crossing over would be decreased and the frequency of nondisjunction increased. However, this hypothesis fails to explain the regular disjunction observed by STURTEVANT and BEADLE (1936) in X chromosomes of the *Drosophila* female made structurally heterozygous by inversion, and therefore unable to undergo intimate pairing and crossing over.

Neither hypothesis can account fully for the phenomenon of "nonhomologous pairing," the occurrence of which was first postulated by COOPER, ZIMMERING and KRIVSHENKO (1955) to explain the increased frequencies of X-chromosome nondisjunction observed in situations where both the X chromosomes and either one of the autosomes were made structurally heterozygous by inversion. Since then SANDLER and NOVITSKI (1956) have postulated the occurrence of pairing between nonhomologues, while the work of GRELL (1957, 1959) and other authors

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(OKSALA 1958, FORBES 1960) have provided convincing genetic evidence that such pairing does occur.

GRELL (1962) noted that in every case where nonhomologous pairing had been reported, it had occurred between chromosomes which were noncrossovers. Furthermore, she found that when one member of a pair of homologues segregated from a noncrossover nonhomologue, the total frequency of crossing over between the homologues remained unaltered. This showed that the homologous chromosomes had had an opportunity to undergo crossing over, but those which had failed to do so were able to enter into later associations with available nonhomologous elements. She concluded that nonhomologues paired in this way could disjoin with the same regularity as homologues, but obviously the kind of pairing involved must be different from pairing for exchange, which, one assumes, can only occur between homologues.

The "distributive pairing hypothesis" therefore recognizes two separate phases in meiosis, involving two distinct kinds of chromosome pairing.

In the first phase, homologous chromosomes pair in preparation for exchange. This is called "exchange pairing" and precedes the second phase in which unpaired chromosomes pair for disjunction. This second type of pairing is called "distributive pairing," and it occurs between homologous or nonhomologous chromosomes, provided they are noncrossovers.

Homologous chromosomes which have undergone crossing over will remain associated by chiasmata at metaphase and disjoin regularly at anaphase I. Chromosomes which have *not* undergone crossing over will enter what GRELL terms "the distributive pool." This pool will be composed of all the available noncrossover chromosomes, which will then have an opportunity to pair with each other and form homologous or nonhomologous partnerships. Chromosomes involved in such partnerships will be just as capable of undergoing regular disjunction as those which are held together by chiasmata.

GRELL (1962) has shown that a single noncrossover in the pool will behave as a univalent and segregate randomly. Two noncrossovers will pair distributively and disjoin with a high degree of regularity. Three noncrossovers compete for partners, and frequency of association between any two of them has been found to be correlated with similarity in length rather than any shared homology (GRELL and GRELL 1960; GRELL 1962, 1964a,b). Thus in a situation with two long elements and one short, the short element is excluded from the pair and segregates randomly. In the case of two short elements and one long, the long element is excluded. For example, in the case of the normal fourth chromosomes, usually noncrossovers, GRELL (1964b) has shown that distributive pairing is the normal mechanism to ensure regular disjunction; the small size of the fours guarding them against involvement with other larger noncrossovers. When one long, one short, and one intermediate element are present in the pool, the long and the short pass to one pole and the intermediate to the other, suggesting directed segregation from a trivalent association. The experiments to be reported here are based on these findings. The results obtained are consistent with the "distributive pairing" hypothesis.

EXPERIMENTAL PROCEDURE

A study has been made of pairing and disjunction in female translocation heterozygotes carrying multiple inversions.

It is known that inversions act as crossover suppressors (STURTEVANT 1926, 1931), and by introducing multiple inversions into the normal homologues of the translocated chromosomes, various numbers of elements can be made available for distributive pairing as noncrossovers. Because of the importance of chromosome size in distributive pairing, the translocations were chosen to provide elements of a variety of different lengths.

Three translocations between the X chromosome and 2R were used: $T(1;2)10 = T(1;2)10B; 50D$; $T(1;2)43 = T(1;2)16B; 60B$ and $T(1;2)69 = T(1;2)3C; 41D$. Translocations 10 and 43 were induced by gamma irradiation and are marked with γ (yellow) and w (white); Translocation 69 was X-ray induced and is marked with γ . They were all obtained by DR. D. L. LINDSLEY at the Oak Ridge National Laboratory.

The translocations were all male sterile and were maintained in balanced lines. The positions of break points, which were confirmed cytologically at the outset of the experiment by salivary chromosome analysis, are shown in Figure 1. Postulated pairing configurations before and after the introduction of inversions are shown in Figure 2.

In order to introduce the multiple inversions, two crosses were made. In the first, females carrying each of the translocations were mated to males of the genotype $\gamma^2/sc^8.Y, SM1/+$. *SM1* is a second chromosome having a long pericentric inversion [*In(2LR)22A3;60B*] superimposed on *In(2L)Cy + In(2R)Cy*. In view of the fact that TINDERHOLT (1961) has reported crossing over in *SM5*, which is rearranged with even more complexity than *SM1*, it is assumed that some crossing over will also take place in *SM1* heterozygotes.

In the second cross, females heterozygous for each of the translocations were mated to males of the genotype *FM6/sc⁸.Y; SM1/+*. *FM6* is an X chromosome having eight breaks and is marked with γ^{31d} (yellow) *sc⁸* (scute), *dm* (diminutive), *B* (Bar). *FM6* virtually eliminates crossing over in the X chromosome. *SM1* was obtained by LEWIS and MISLOVE (1953); *FM6* was obtained by GRELL and LEWIS (1956).

From these crosses four kinds of females were obtained for each translocation. These were heterozygous for the translocation, and had: (1) no inversions present; (2) *SM1* present; (3) *FM6* present; and (4) *SM1* and *FM6* present.

In Translocation 10, the γ^2 chromosome was replaced by an X chromosome carrying the markers $\gamma^2 sc v f$ (yellow, scute, vermilion, forked). The purpose was to introduce vermilion to mark the break point of the translocation, but the presence of the other markers made it possible to measure crossing over throughout most of the X chromosome. In Translocation 43 a

FIGURE 1.—Location of breakpoints in the three translocations given the code numbers 69, 10, and 43.

normal X chromosome marked with γB (yellow, Bar) was introduced. Normal progeny could thereby be distinguished from progeny carrying the translocation.

Females from each of the four groups were then crossed to normal males of an appropriate genotype so that all regular progeny, normal or heterozygous for the translocation, and the viable half of the X-exceptions could be recognized.

Viable progeny are produced when both halves of the translocation or both the normal unchanged homologues are recovered together in the oocyte. Progeny nondisjunctive for the X chromosomes are produced when both halves of the translocation plus the untranslocated X chromosome pass together to one pole and the untranslocated chromosome 2 goes alone to the opposite pole.

RESULTS AND ANALYSES

From this point on, the symbols T_x and T_2 will be used to designate the two parts of the reciprocal translocation. T_x represents the X-centric and T_2 the 2-centric element in the translocation. X and 2 will be used to designate the unchanged chromosomes.

As stated earlier, X-exceptions are produced when T_x , T_2 , and X are recovered together at one pole while 2 goes alone to the opposite pole. Such 3:1 disjunction should result from half the cases in which chromosome 2 forms a trivalent association with and segregates from any two of the three remaining elements. The

FIGURE 2.—Postulated pairing configurations before and after the introduction of multiple inversions into the homologues of the translocated chromosomes. Crosses indicate arms in which crossing over is expected. The abbreviations T_x and T_2 refer to the two halves of the translocation. T_x has the centromere of the X chromosome and T_2 has the centromere of chromosome 2. Solid lines represent normal and translocated X chromosome segments; broken lines represent normal and translocated second chromosome segments; looped lines represent multiply inverted X and second chromosome segments. Large numbers under each figure represent the number of available noncrossovers in the distributive pool.

trivalent may be formed at the time of exchange pairing or distributive pairing. In the first case, however, segregation, will be determined by chiasmata, while in the second case it will be determined by the size of the various elements involved.

Situations which will *not* give X-exceptions are those in which 2:2 segregation occurs. This will be expected when no elements are present in the distributive pool, or when two elements are present so that a bivalent of crossovers and a bivalent of noncrossovers are formed, or when four elements are in the pool and distributive pairing is such that two bivalents of noncrossovers are formed.

These simple postulated behaviors in an exceedingly complex situation represent just a few of the possible configurations and segregations which may in fact occur.

The frequencies of nondisjunction obtained are interpreted using predictions made in the distributive pairing hypothesis. The results can only be dealt with in such a way as to see to what extent these predictions apply to segregation in translocation heterozygotes. No attempt can be made to ascertain the exact type of segregation in each situation, firstly because of the lack of markers and secondly because there is no way of recovering inviable products of oogenesis when the male translocation heterozygote is sterile.

Table 1 shows how the nondisjunction rate varies from one situation to another for each translocation. The final percentage nondisjunction is estimated by doubling the actual frequency of exceptional progeny. All estimates are based on 2,000 or more flies.

Before the introduction of inversions (see Figure 2) Translocation 69 gave 9.7% nondisjunction. Perhaps the reason for this is that crossing over in the interstitial region of the X is reduced owing to translocation of the distal tip, and whenever X is a member of the distributive pool as a noncrossover it is the only member because T_x is tied up by crossing over with 2. Segregation from the trivalent would be expected to give T_2 and T_x to one pole.

When *SM1* was introduced, nondisjunction fell to 3.3%. From Figure 2 it can be predicted that when *SM1* is present, two elements will be liberated into the distributive pool with a high frequency—a situation which will not favor the production of X-exceptions. Furthermore, the chances of obtaining 3:1 segregation are lower than in the controls because the presence of the inversion in chromosome 2 will tend to increase crossing over in the X chromosome (Dob-

TABLE 1

Percentage X chromosome nondisjunction for each translocation, before the introduction of inversions, and with SM1 and/or FM6

Translocation	+, +	+, <i>SM1</i>	<i>FM6</i> ; +	<i>FM6</i> ; <i>SM1</i>
69	9.7	3.3	27.5	5.9
10	5.6	3.9	23.9	7.8
43	10.7	4.4	5.5	17.0

ZHANSKY and STURTEVANT 1931). Crossing over in the X chromosome could not be measured because of the lack of markers.

In the presence of *FM6*, nondisjunction rose to 27.5%. From Figure 2 it can be seen that crossing over is expected in 2L and 2R, but crossing over in the X chromosome will be virtually eliminated. Thus there will be only one element in the distributive pool—namely *FM6*, which by segregating randomly can give X nondisjunction when recovered together with T_x and T_2 .

When both *SM1* and *FM6* were present the rate of nondisjunction was lower than the control value. In this case, there will be four noncrossovers in the distributive pool and pairing might be expected to follow the rules of the distributive pairing hypothesis concerning the importance of size. If so, one expects X to pair with T_2 and T_x to pair with 2. As stated before, the formation of two bivalents will give two-by-two segregation and X-exceptions will be recovered with a low frequency.

Translocation 10 gave the lowest frequency of nondisjunction among the three translocations, before the introduction of inversions. Some measure of crossing over in the X chromosome was obtained owing to the presence of markers. In the region *w-v* it was 14.5% and in the region *v-f* it was <1%. Because of this low rate of crossing over, there is a good chance that X and T_x will be present as noncrossovers in the pool to pair distributively and segregate to opposite poles. Whenever this happens, the recovery of T_x , T_2 , and X together at one pole (necessary for the production of an X-exception) is made impossible.

When *SM1* was introduced into Translocation 10, nondisjunction fell below the control value. Crossing over in the region *w-v* rose to 22.9% and in the region *v-f* it rose to 3%. Again, the presence of the inversion in chromosome 2 was increasing crossing over in the X chromosome, thus reducing the chances of having the X chromosome present as a univalent in the pool. Since crossing over between *v* and *f* was still only 3%, the chances of there being two elements present in the distributive pool was high, and so nondisjunction rate was low.

With *FM6* however, nondisjunction rose to 23.9%. It can be seen from Figure 2 that *FM6* was the only element in the distributive pool and would segregate randomly as a univalent. T_x should be present in the pool also more often than in Translocation 69, thus cutting down nondisjunction slightly. The results bear out this prediction. Segregation from the remaining three elements would be expected to send T_x and T_2 together to one pole if crossing over occurred in both 2L and 2R.

In the presence of *SM1* and *FM6*, the nondisjunction rate stayed low. It is postulated that pairing occurred between X and T_x and between 2 and T_2 , the pairing occurring between elements of closely similar size. Thus two-by-two segregation was expected.

In Translocation 43, before inversions are introduced, it is expected that the chances of the small T_x element being present in the pool will approach unity and the chances of its being there alone will be high. Crossing over in the region *w-B* was found to be 28.5%, and so the X chromosome is expected to be a member of the pool with a frequency of approximately 50%. When both T_x and X are in

the pool, X-exceptions will not be recovered because of distributive pairing between them. When T_x is alone in the pool, i.e., with an expected frequency of 50%, one would expect the nondisjunction rate to approach 25%. Instead the rate of nondisjunction is only 10.7. However, it has been stated earlier that the presence of a univalent in the pool is not alone sufficient to cause an increase in nondisjunction. There must also be an appropriate segregation of the three remaining elements. In this case, if crossing over occurs in the X and 2R, segregation from the X, T_2 , 2 trivalent will be expected to send X and T_2 to opposite poles. That this is not always the case is evidenced by the recovery of seven equational exceptions which were homozygous γw . They show that segregation from the trivalent can be such that T_2 and X move to the same pole, despite crossing over. Owing to crossing over in the interstitial region of 2R it may be the centromere of T_2 or the centromere of 2 which goes with X. RHOADES (1933) has postulated that there is a positive correlation between crossing over near the centromere and disjunction to opposite poles, and perhaps the equational exceptions are produced when crossing over has occurred near the distal tip of X and segregation has been determined by chiasmata situated near the centromere in 2. Actually, the recovered equational exceptions only represent a portion of those occurring, since the X chromosome was inadequately marked to detect others.

In the presence of *SM1*, crossing over in the region w -*B* rose to 42.3%. Low nondisjunction was expected and found because there were two elements in the pool—the T_x fragment and *SM1*. In the presence of *FM6*, the level of nondisjunction was again low because two elements were present in the pool. When both *SM1* and *FM6* were present, nondisjunction rose to 17%. Here one can postulate some trivalent-univalent formation, since the four elements show great diversity in length. If the three largest elements formed a trivalent from which the large (T_2) and the small (X) segregated to one pole, there would be a good chance of recovering these two together with the T_x at one pole.

One further point of interest in the data was the occurrence of nonrandom disjunction. It can be seen from Table 2 that in Translocation 69 the ratio of normal progeny (N) to progeny carrying the translocation is approximately 2:1 when the normal X chromosome is free from inversion (lines 1 and 2). In the presence of *FM6* (lines 3 and 4) the ratio is the expected 1:1 for random segregation.

This excess of normal progeny appears to be due to "nonrandom disjunction," a phenomenon first described by NOVITSKI (1951) and later studied in female translocation heterozygotes by ZIMMERING (1955). NOVITSKI found that when two structurally different chromatids making up a dyad disjoined at the second meiotic division there was a marked deviation from the normal 1:1 expectation of recovery of complementary types. Nonrandom disjunction favored the inclusion into the egg nucleus of a short chromatid rather than its complementary long chromatid. Genetic analysis showed that the inequality of the two complementary classes arose after exchange had occurred giving asymmetrical dyads.

In Translocation 69, the phenomenon of nonrandom disjunction appears to favor the inclusion of the smaller, normal X chromatid more often than the larger

TABLE 2

Total progeny from the three translocations

	Genotype	T* ♀♀	N† ♀♀	T ♂♂	N ♂♂	XXY	X0	Total
Translocation 69								
1	$\frac{T}{\gamma^2}; +$	529	975	468	1081	62	101	3216
2	$\frac{T}{\gamma^2}; SM1$	482	809	354	726	10	30	2411
3	$\frac{T}{FM6}; +$	800	813	672	671	245	316	3517
4	$\frac{T}{FM6}; SM1$	894	885	687	725	32	65	3288
Translocation 10								
1	$\frac{T}{\gamma^2 sc v f}; +$	1777	1646	1164	1626	87	89	6389
2	$\frac{T}{\gamma^2 sc v f}; SM1$	930	1055	569	903	31	38	3526
3	$\frac{T}{FM6}; +$	822	809	469	708	202	239	3249
4	$\frac{T}{FM6}; SM1$	609	598	333	431	37	46	2054
Translocation 43								
1	$\frac{T}{\gamma B}; +$	822	1157	638	801	61	143	3622
2	$\frac{T}{\gamma B}; SM1$	658	814	622	615	29	33	2771
3	$\frac{T}{FM6}; +$	718	918	579	766	17	70	3068
4	$\frac{T}{FM6}; SM1$	501	507	441	368	53	116	1986

* T=Translocation heterozygotes.

† N=Normal progeny.

T_x chromatid when there is good opportunity for crossing over in the interstitial region of the X chromosome. When crossing over is prevented by the introduction of *FM6*, the effect of nonrandom disjunction disappears.

Translocation 43 exhibits the same phenomenon, but in this case crossing over in the interstitial region of 2R is responsible for the production of unequal dyads—*SM1* eliminates the effect.

In Translocation 43, nonrandom disjunction should effect the exceptional progeny as well as the regulars, since the production of an unequal dyad depends on crossing over in chromosome 2 rather than in the X chromosome. However, if, as we have supposed, X-exceptions are formed when the X chromosome segregates randomly as a noncrossover, the effect of nonrandom disjunction should not be reflected in the exceptional progeny of Translocation 69. In the absence

of crossing over in the X chromosome, unequal dyads will not be produced. Nevertheless, in Translocation 69, there is an excess of X0 males to XXY females in the control series which is still present to a lesser extent after the introduction of *FM6* and is very obvious after the introduction of *SM1* and *FM6* in combination. Also, in Translocation 43, there is still an excess of X0 males when both inversions are present in combination, even though the effect of nonrandom disjunction has been wiped out in the regular progeny.

At the present time, no explanation can be offered for these discrepancies.

DISCUSSION

The various hypotheses put forward to explain the relation between crossing over and disjunction in heterozygous translocations in the *Drosophila* female have been discussed at length by BROWN (1940). Although her discussion is limited to problems of segregation in autosomal translocations, where recovery of nondisjunctional products is dependent also on segregation in the male translocation heterozygote, some of her conclusions are relevant to the present discussion concerning X chromosome nondisjunction.

Her main conclusion was that disjunction was correlated with chiasma formation. When no chiasmata were formed in a translocated chromosome, it segregated at random and caused an increase in nondisjunction. Earlier, DOBZHANSKY (1932, 1933) had concluded that disjunction in the female was determined by intimacy of pairing before crossing over and disjunction. He had tested the effects of inversions on disjunction in females heterozygous for 2;3 translocations and had found that the presence of an inversion in chromosome 2 caused a suppression of crossing over and an increased frequency of nondisjunction. He concluded that chromosome 2 was segregating randomly as a univalent because pairing had been disrupted by the presence of the inversion.

From the results of the present studies, it is clear that the chiasmata are responsible for determining disjunction in crossover chromosomes, but orderly disjunction can also occur in noncrossovers, as predicted on the distributive pairing hypothesis. It can be seen that when the X chromosome alone is prevented from undergoing crossing over by the presence of *FM6*, it behaves as a univalent and segregates randomly with respect to its homologue involved in the translocation. The increased frequency of X chromosome nondisjunction in Translocations 69 and 10 in the presence of *FM6* gives proof of this. However, when a second noncrossover is available for pairing with the X chromosome, e.g., T_x in Translocation 43, nondisjunction actually falls below the control value.

As crossing over increases in the X chromosome, e.g., by the introduction of *SM1*, the chances of the X chromosome being present in the distributive pool as a randomly segregating element are decreased. For all of the translocations, when *SM1* is introduced, two elements are present in the distributive pool and the nondisjunction rate falls below the control value. It is concluded that two bivalents are formed, one bivalent of crossovers associated by chiasmata and one bivalent of noncrossovers, and that orderly two-by-two segregation follows.

When both *FM6* and *SM1* are present in combination, crossing over is suppressed in all the four arms of the translocation figure, and pairing is expected to be determined by size of the elements. If at least two of the four elements are closely similar in size, two bivalents should be formed and nondisjunction should be low. If the four elements show great diversity in length some trivalent-univalent formation may occur and nondisjunction should increase. In fact the results indicate that this may be occurring. Translocations 69 and 10, in which there is close similarity in length between pairs of elements, give no increase in nondisjunction while Translocation 43, in which the elements differ in length from each other, shows an increased nondisjunction rate. However, it must also be considered that trivalent-univalent and bivalent formation are not the only situations possible when four elements are present in the pool. There may also be multivalent formation which may not give a strongly directed segregation, and this possibility lies between the two extremes that are postulated.

Since the first draft of this paper, NOVITSKI (1964) has proposed a model to account for the pairing and disjunction of nonhomologous chromosomes at meiosis in the female of *D. melanogaster* which assumes the existence of "an association of the centromere regions and adjacent heterochromatin of all the chromosomes in a chromocentral configuration, prior to the time of synapsis and crossing over." It is implied that the karyosome described by KING, RUBINSON, and SMITH (1956) is the cytological manifestation of this chromocentre in the oocyte nucleus.

NOVITSKI, then postulates that homologous chromosomes associated in the chromocentre would synapse, undergo exchange and then "leave the chromocentre as independent bivalents." All the chromosomes remaining at the chromocentre (all the noncrossovers) would then be free to associate with each other in homologous or nonhomologous associations. He suggests that the association of chromosome tips could provide a simple means by which noncrossover chromosomes might associate according to size.

Although this hypothesis is presented as "an alternative to the Distributive Pairing hypothesis," a close study reveals that NOVITSKI's proposed sequence of chromosome pairing (as opposed to general association in a chromocentre) is in accord with that postulated by GRELL, and would be expected to produce the same genetic results. While GRELL is noncommittal over the site or time of the pairing between nonhomologous chromosomes, except that it follows homologous pairing ("exchange pairing"), NOVITSKI postulates that all pairing occurs at the chromocentre. Such a postulate is not supported by cytological evidence.

It is open to question whether the chromocentral configuration, represented by the karyosome in the oocyte nucleus is in fact present "prior to the time of synapsis and crossing over." Stage 3 oocyte nuclei are the first to show a Feulgen positive karyosome (KING, RUBINSON and SMITH 1956) while genetic studies on the effect of various agents on crossing over (PLOUGH 1917; CHANDLEY and BATEMAN 1953; GRELL and CHANDLEY 1965) indicate that crossing over occurs at an earlier stage than this. The most recent data (GRELL and CHANDLEY 1965) indicate that it takes place at or near the time of DNA synthesis in 16-cell cysts situated in the germarium.

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SUMMARY

Chromosome pairing and disjunction have been studied in female translocation heterozygotes carrying multiple inversions. The results are interpreted on R. GRELL's hypothesis of "distributive pairing." Three translocations involving ex-

change between the X chromosome and the right arm of chromosome 2 were chosen deliberately to form a series giving a variety of arm lengths due to reciprocal exchange. The use of the multiply inverted chromosomes *FM6* and *SM1*, either singly or in combination, as the homologues of the translocated X and second chromosome, served to suppress crossing over in various arms and make noncrossovers available for distributive pairing.

Results showed a significant increase in X chromosome nondisjunction when *FM6* was the only noncrossover in the pool. When a second noncrossover was available to pair distributively with *FM6*, the level of nondisjunction fell below the control value. When four noncrossovers were made available for distributive pairing by the introduction of both *FM6* and *SM1*, a significant increase in X chromosome nondisjunction was found in Translocation 43. It was a translocation in which the four elements showed great diversity in chromosome length. Some trivalent formation is postulated to account for the increase in nondisjunction.

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