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Genetics

Synapsis-dependent allelic complementation at the decapentaplegic gene complex in *Drosophila melanogaster*

(transvection/gene organization/gene regulation/somatic chromosome pairing/chromatin structure)

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ABSTRACT **Allelic complementation at the decapentaplegic gene complex (*dpp*: 2-4.0, cytogenetic location: polytene chromosome bands 22F1-3) of *Drosophila melanogaster* frequently occurs between site mutations. Two specific instances of allelic complementation are shown to be dependent upon normal somatic chromosome synapsis of homologous *dpp* genes. Numerous strains have been identified that bear lesions that disrupt allelic complementation when heterozygous with structurally normal chromosomes; each of these 57 strains contains a gross chromosomal rearrangement with a break on chromosome 2. The properties of the rearrangements carried by 50 of these strains are consonant with the idea that their effects are due to a disruption of somatic chromosome synapsis in the *dpp* region of chromosome arm 2L. In double heterozygotes of simple two-break rearrangements, allelic complementation is restored (presumably through the restoration of structural homozygosity). The types of rearrangements that disrupt complementation have properties very similar to those of rearrangements that disrupt the transvection effect at bithorax [Lewis, E. B. (1954) *Am. Nat.* 88, 225–239]. The existence of synapsis-dependent allelic complementation is a demonstration of the physiological importance of nuclear organization in gene expression.**

Somatic chromosome synapsis between homologues is well known in dipteran insects. The most obvious examples of this phenomenon are the polytene chromosomes found in the nuclei of a variety of specialized cell types. In addition to being endoreplicated, homologues are aligned and paired in exact register. While the physiological significance of somatic chromosome synapsis remains unclear, a few instances of synapsis-dependent phenotypes have been reported in *Drosophila melanogaster* (1–4). "Transvection" is the term coined by Lewis (1) to describe the phenomenon of synapsis-dependent allelic complementation at the bithorax locus. Allelic complementation occurs in genotypes in which somatic chromosome pairing of the bithorax alleles is unhindered, whereas complementation is not found in genotypes in which chromosomal rearrangement heterozygosity interferes with such pairing. Synapsis-dependent gene expression also has been demonstrated in the zeste–white system (2), but it appears not to involve allelic complementation.

During investigation of the decapentaplegic gene complex in *D. melanogaster*, allelic complementation between site mutations was noted. In this report, allelic complementation at decapentaplegic is demonstrated to be a transvection effect. As in the bithorax system, structural heterozygosity disrupts complementation. The cytogenetic properties of rearrangements disrupting complementation at decapentaplegic and at bithorax are very similar. A molecular model of transvection is considered.

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MATERIALS AND METHODS

Mutations. With the exception of the decapentaplegic alleles described in the text, all mutations and balancer chromosomes are described in Lindsley and Grell (5).

Culture Conditions. Flies were cultured on standard *Drosophila* cornmeal/yeast extract/sucrose medium in half-pint milk bottles or 25 × 95 mm shell vials. Progeny of all crosses were reared at 25°C.

Mutagenesis Procedures. X-irradiation was performed with a Keleket 250-kV x-ray machine at maximal voltage with no filters. X-rays were delivered at dose rates of 350–400 roentgens/min. Males were aged for several days, irradiated, and allowed to mate with tester females for 1 day. The males were then separated and discarded; inseminated females were allowed to lay eggs on fresh medium for two 3-day transfers.

Wing Angle Measurements. The phenotype being studied affects the orientation of the wings relative to the body of the fly. To quantitate the phenotypes of various mutant genotypes, the angle each wing made to the long axis of the body was measured on a standard grid dividing a 90° arc into six 15° sectors. In general, an average measurement for a given genotype is based on the scoring of at least 30 individuals (60 wings).

RESULTS

The decapentaplegic locus (*dpp*: 2-4.0) occupies all or a portion of polytene chromosome bands 22F1-3 near the distal tip of the left arm of chromosome 2 (abbreviated 2L) (6). Decapentaplegic mutant individuals characteristically exhibit pattern defects in structures derived from one or more imaginal disks. The alleles we will be concerned with are dpp^{ho} (formerly *ho*, heldout), dpp^{ho2}, and dpp^{4}. All three of these recessive alleles are cytologically normal and have a common phenotype of held-out wings (dpp^{ho}, dpp^{ho2}) or wing stumps (dpp^{4}). (dpp^{4} affects the wings more severely than do the other two alleles, and it also affects structures derived from other imaginal disks; these effects are not relevant to the present discussion.) As shown in Table 1, each allele can cause a fly's wings to be held out laterally instead of being oriented at rest along the longitudinal axis of the body. However, two heterozygotes (dpp^{ho}/dpp^{4} and dpp^{ho2}/dpp^{4}) have normally oriented wings. It is the allelic complementation of these heterozygotes that we have hypothesized to be synapsis dependent.

The transvection hypothesis was developed as one part of a formal model of the organization of the *dpp* gene complex. In this model, designed to account for the phenotypic interactions of our various *dpp* alleles, we visualize *dpp* as representing a multigene cluster, with different genetic elements within the

Abbreviations: DTD, decapentaplegic transvection-disrupting rearrangement; BTD, bithorax transvection-disrupting rearrangement.

Table 1. Wing phenotypes of various *trans* heterozygotes of the type dpp^x/dpp^y

	dpp^x				
dpp^y	dpp^{ho}	dpp^{ho2}	dpp^4	dpp^R*	dpp^+
dpp^{ho}	Ho	Ho	+	Ho	+
dpp^{ho2}		Ho	+	Ho	+
dpp^4			Lethal†	Ho‡	+
dpp^R				Ho‡	+
dpp^+					+

Ho, heldout wings; +, normally oriented wings.
* dpp^R alleles are a large class of extreme x-ray-induced *dpp* alleles associated with gross chromosomal rearrangements sharing a breakpoint in 22F1-3 (6).
† dpp^4 homozygotes die as embryos (7).
‡ In addition to being held out, these wings are reduced in size (6).

cluster controlling the development of different regions of all imaginal disks. There is a polarity of expression of functions within this cluster, with the dpp^{ho+} element representing a function downstream from most elements (including the one containing the dpp^4 alteration). *Trans* complementation of dpp^{ho} with ethyl methanesulfonate-induced site mutations such as dpp^4 is disquieting because each allele generates flies with held-out wings when heterozygous with alleles of the more extreme rearrangement-bearing dpp^R type (Table 1). Transvection (i.e., synapsis-dependent allelic complementation) can explain the different behaviors of site mutant and rearrangement mutant heterozygotes. In such a heterozygote, the heldout phenotype of the rearranged *dpp* allele was viewed as a composite of (*i*) the lesion due to the break itself, (*ii*) the polar effects exerted as a consequence of the separation of the regions of the complex proximal and distal to the breakpoint, and (*iii*) the synapsis-disruption in the vicinity of the breakpoint. In addition transvection helps to explain why ethyl methanesulfonate, which is primarily a point mutagen, is ineffective in generating mutations allelic to dpp^{ho}.

If complementation between *dpp* site mutations is synapsis dependent, then by definition it should not occur if somatic chromosome pairing is disrupted in distal 2L, where *dpp* resides (22F1-3). Heterozygosity for some subset of rearrangements of chromosome arm 2L that disrupt pairing in the decapentaplegic region ought to interfere with complementation. Flies that are heterozygous for such rearrangements and that are dpp^{ho}/dpp^4 or dpp^{ho2}/dpp^4 should be detectable as heldout individuals.

To produce and identify such rearrangements, dpp^{ho}/dpp^4 and dpp^{ho2}/dpp^4 F_1 individuals were generated from x-irradiated fathers crossed to appropriate tester females (Table 2). These F_1 flies were scored for wing orientation. Flies having both wings held out at least 45° were classified as strongly heldout, whereas flies in which only one wing was held out or in which both wings were held out less than 45° were classified as moderately heldout.

In these experiments, all of the strongly heldout and some of the moderately heldout flies were mated to appropriate testers and their progeny were scored. Lines containing reliable heldout phenotypes either exhibited segregation with the second chromosome or had dominant mutations mimicking heldout; these latter mutations were not analyzed further. The mutations linked to chromosome 2 were placed into balanced stocks and characterized (*i*) with regard to the state of the *dpp* locus to ensure that the original *dpp* allele was still present and (*ii*) for the presence of chromosomal rearrangements. The heldout phenotype associated with each of these lines was quantitated.

Fifty-seven strains that dramatically disrupt allelic complementation have been analyzed. In these strains, complementation disruption varies significantly from one line to another. In all but the most extreme lines (in which all flies have 90° heldout wings), expression is variable. Occasionally, we encounter an individual with one completely normal wing and the other 90° held out.

Fifty-six of the 57 strains contain gross chromosomal rearrangements involving chromosome arm 2L! Their other breakpoints can involve any of the other chromosome arms in the genome, but only with 2L is there a strong correlation with complementation-disruption. Thus, the initial transvection prediction obtains. The remainder of the observations will focus on the following questions. What types of rearrangements disrupt allelic complementation? Is the disruption of complementation associated with structural heterozygosity, implying interference with somatic chromosome synapsis?

Patterns of Chromosomal Rearrangements Disrupting Allelic Complementation. Of the 57 complementation-disrupting rearrangements (which we will abbreviate DTDs for decapentaplegic transvection-disruptors) 15 are derived from experiment 1, 5 from experiment 2, 7 from experiment 3, and 30 from experiment 4. They may be classified as follows:

(a) *Simple DTDs with one break in 22F3 to 35E and a second break in a proximal region of another chromosome arm.* Thirty-six two-breakpoint simple DTDs were recovered. Five are exceptional DTDs considered in Section *c*. Thirty-one (Fig. 1, open circles) can be categorized as follows: a break in 2L within the region of 22F4 to 35E is joined with a break in a proximal region of some other chromosome arm (within two polytene chromosome divisions of its chromocentral connection). The proximal break can be in virtually any other chromosome arm (0 in X, 4 in Y, 0 in 2L, 12 in 2R, 2 in 3L, 5 in 3R, and 8 in 4). The paucity of breaks involving the sex chromosomes is probably not significant. During stock construction, only male-fertile lines were saved. Because most X–2 translocations (7) and approximately half of all Y–2 translocations (8) are male-sterile, it is not surprising that these rearrangements are underrepresented.

The chromosome arm to which a 2L breakpoint is attached

Table 2. Results of screening for complementation-disrupting lesions

Exp.	Male parent	Female parent	No. heldout (%) Strong	No. heldout (%) Moderate	Total Cy^+
1	$dpp^4/In(2LR)Cy0$	*ast* dpp^{ho} *ed dp cl*	81 (1.6)	34 (0.7)	5173
2	$dpp^4/In(2LR)Cy0$	*ast* dpp^{ho} *ed dp cl*	32 (1.3)*	39 (1.6)	2421
3	*ast* dpp^{ho} *ed dp cl*	$dpp^4/In(2LR)Cy0$	13 (0.9)	34 (2.4)	1432
4	dpp^{ho2}	$dpp^4/In(2LR)Cy0$	71 (2.3)	73 (2.4)	3064

Males were x-irradiated with 4500 rads and mated to appropriate tester females such that dpp^4/dpp^{ho} or dpp^4/dpp^{ho2} offspring were generated. Cy^+ progeny were scored for wing position. All individuals with strongly heldout wings and some of those with moderately heldout wings were saved for further analysis. The numbers in parentheses are the percentages of total Cy^+ offspring in each heldout class.
* Two of these heldout individuals turned out to be newly induced *dpp* alleles superimposed on dpp^4.

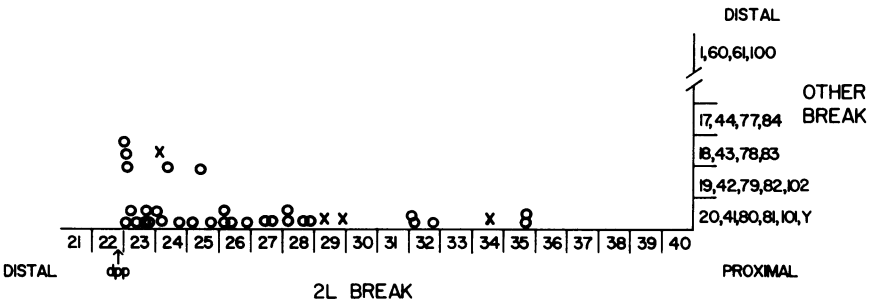

FIG. 1. Polytene chromosome distribution of the breakpoints of 35 DTDs. The abscissa represents the standard polytene divisions along chromosome arm 2L and the ordinate represents the proximal regions of all other chromosome arms. The Y chromosome is considered entirely chromocentral (proximal) on the representation. ○, Breakpoints in 31 class *a* two-break rearrangements disrupting allelic complementation at *dpp*. ×, Four more complex rearrangements similarly bringing distal 2L to a proximal location.

seems to dramatically affect its ability to act as a DTD (Fig. 2). The only DTDs of proximal 3L that have been recovered have 2L breaks within one division of *dpp*. In fact, two other rearrangements of 2L reattached to proximal 3L produce no complementation-disrupting effects [T(2;3)23D1-2; 80F; and T(2;3)33E-F; 80F]. In contrast, DTDs that are rearrangements joining 2L to proximal 2R or to chromosome 4 are recovered frequently and can have their 2L breakpoints anywhere within a large region proximal to *dpp* (23A1 to 34D and 22F4 to 35D-E). Y breakpoints, while recovered infrequently, also extend over a large region of 2L (23A to 35D-E). DTDs involving proximal 3R seem to behave in an intermediate fashion, with their 2L breaks being only as proximal as section 27 or 28. As with 3L, we have independently recovered reciprocal translocations involving 3R with more proximal 2L breakpoints; these are without complementation-disrupting effect.

(b) *Complex DTDs: Insertional translocations and transpositions.* Eighteen complex DTDs have properties consistent with effects on chromosome synapsis. Seven involve breaks in the 22F and 35E region that bring distal 2L near the proximal region of another chromosome arm. The other 11 of the complex DTDs are insertional translocations or transpositions of a piece of 2L including the *dpp* locus. That is, in each of these 11 cases there is both a breakpoint distal to *dpp* (in 21A to 22E) and one proximal to it (in 23A to 40F). The chromosomal fragment containing *dpp* is inserted into a medial or proximal position on another chromosome arm. The break proximal to *dpp* apparently can be located anywhere on 2L. Breaks as near to *dpp* as 22F4–23A1 or as far away as 40F have been recovered among these complex DTDs.

(c) *Exceptional DTDs.* Eight DTDs do not fall into either of the two previous categories. One is a large paracentric inversion of 2L with breakpoints in 21B and 40F; its structure is consistent with a *dpp* synapsis-disrupting rearrangement (see *Discussion*). The other seven are not easily interpreted as such. Six have breaks on 2L but do not severely impair synapsis of this arm, at least in polytene chromosomes (data not shown). Three of these have a breakpoint in or near 90A. No other repeating breakpoints are noted among these rearrangements. The eighth rearrangement is not broken at all on 2L; it is the only such rearrangement encountered in this study. Curiously, its 2R breakpoint is located within the 5S rRNA-coding region in 56F (9). Part of the 5S rDNA array is inserted into the centric heterochromatin of chromosome 4.

Structural Heterozygosity Is the Basis for Disruption of Allelic Complementation. In principle, the rearrangements disrupting complementation may act in one of two ways. They may disrupt synapsis of the two *dpp* alleles as has been proposed, or, due to alteration of loci at or near the breakpoints, they may behave as genic mutations which are dominant enhancers of the *dpp* heldout phenotype. The distribution of DTD breakpoints in general supports the model of synapsis disruption. Notably, 56 of the 57 DTDs have breakpoints distributed continuously on 2L. If these represented dominant enhancer mutations, it seems unlikely that so many of them should be associated with breakpoints on this chromosome arm. Also, if these strains were all carrying dominant enhancer mutations, some ought to be associated with site mutations or simple deletions. The distribution of DTD breakpoints on chromosome 2 is certainly nonrandom. For example, in control experiments to be described elsewhere, random translocations between chromosomes 2 and 3 more often involve breaks on 2R than on 2L. Only half of the T(2;3) breaks on 2L fall into the *dpp* critical region and only one-fourth of the breaks on 2R are very proximal.

To critically distinguish the two models, let us consider the simple rearrangements with one breakpoint in 22F4 to 35D-E and the other in the proximal region of another chromosome arm (class *a*). If the rearrangements represent dominant enhancer mutations, then double heterozygotes or homozygotes for such enhancers ought to be at least as extreme in phenotype as are the *DTD*/+ single heterozygotes. On the other hand, if the rearrangements act by disrupting synapsis in the *dpp* region, homozygosis of a particular rearrangement should restore synapsis and complementation. If the breakpoints of double heterozygotes are sufficiently similar to one another, then they too should restore synapsis and complementation. Because many of the simple class *a* rearrangements have similar breakpoints on 2L and are broken in proximal regions of other chromosome arms, it has been possible to construct a number of double heterozygotes of the type $DTD_a\ dpp^{ho2}/DTD_b\ dpp^4$. (By using double heterozygotes, we circumvent any recessive

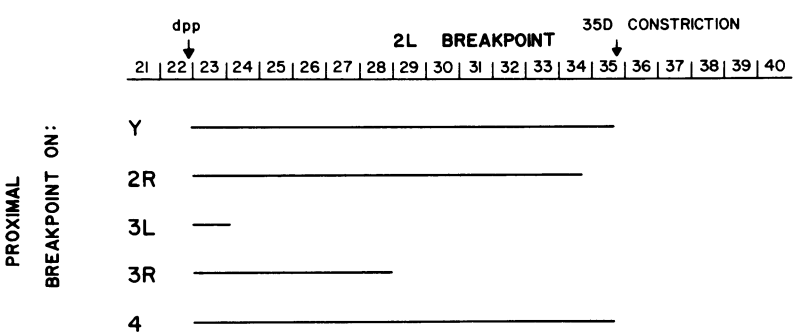

FIG. 2. Distributions of 35 DTD 2L breakpoints arranged by chromosome arm of the other breakpoint. The abscissa represents the 2L polytene division and each line represents the range of rearrangement breakpoints reattached to the proximal region of the indicated chromosome arm.

Table 3. Wing positions of $DTD_a\ dpp^{ho2}/DTD_b\ dpp^4$ double heterozygotes

		$DTD_a\ dpp^4$						
DTD_b dpp^{ho2}	Breakpoints	*DTD15* 22F3-4; 102F	*DTD8* 23D1-2; 41A	*DTD13* 24A1-2; 101A-D	*DTD24* 26C1-2; 41A	*DTD11* 28A; 41A	*DTD4* 32E1-2; 41A-C	dpp^4 None
DTD36	23D1-2; 81F	A	B	A	A	B	F	E
DTD42	23E1-2; 41	A	A	A	A	A	C	D
DTD39	24C; 102B	A	A	A	A	A	E	E
DTD52	24E; 41	A	A	A	A	A	D	D
DTD40	25C; 102B	A	A	A	A	A	D	E
DTD32	26A; 41	A	A	A	A	A	D	C
DTD46	26F; 81F	A	D	B	A	A	D	E
DTD51	27D1-2; 41A-B	A	A	A	A	A	C	D
DTD37	28D; 101A	A	B	A	A	A	E	E
DTD38	29B; 101A*	A	C	A	B	A	D	E
DTD55	32A1-2; 41A	E	E	E	B	B	D	D
DTD43	34D; 41A†	F	F	F	E	F	F	E
dpp^{ho2}	None	E	F	F	D	E	D	A

The double heterozygotes were generated from crosses of $DTD_a\ dpp^{ho2}/In(2LR)Cy0$ females by $DTD_b\ dpp^4/In(2LR)Cy0$ males. The angles at which each individual's wings were held were measured on a standard grid divided into six sectors at 15° each. The letters *A–F* represent the average wing angle for a given genotype and each average is based on at least 60 wing measurements. *A* represents an average held-out wing angle of 0–15° (i.e., wild-type), *B* of 15–30°, *C* of 30–45°, *D* of 45–60°, *E* of 60–75°, and *F* of 75–90° (extreme heldout).

* + *In(2L)* 29B; 32A.

† + *T(2;3)* 57E-F; 84A-B.

lethality associated with rearrangement breakpoints as well as recessive modifiers of wing position.) Double heterozygotes were generated by all possible crosses of 12 $DTD_a\ dpp^{ho2}$ strains to 6 $DTD_b\ dpp^4$ strains (Table 3).

Virtually all double heterozygotes with breakpoints in the distal half of 2L exhibit a partial or full restoration of complementation. Double heterozygotes with breakpoints as distant as 22F3-4 and 29B exhibit full complementation [*T(2;4)DTD15/T(2;4)DTD38*] even though each single heterozygote is characterized by wings held out 60–75°. Even with rearrangements joining distal 2L to proximal regions of different chromosome arms (e.g., *In(2LR)DTD11/T(2;4)DTD38*) complementation occurs. The only exceptions involve rearrangements with relatively separate 2L breakpoints in which reattachment has occurred to different proximal arms. The rearrangement with a break in 32A, *In(2LR)DTD55*, does not restore complementation in combination with the most distally broken 2L rearrangements. Note that DTDs with the most proximal breakpoints on 2L [*In(2LR)DTD4* and *In(2LR)DTD43*] exhibit no restoration of complementation in combination with any of the more distal DTDs or with each other.

DISCUSSION

Allelic complementation at *dpp* is clearly a synapsis-dependent transvection effect. Complementation is disrupted by the presence of specific sorts of heterozygous rearrangements of chromosome arm 2L. Similarly, as will be described elsewhere, many of these rearrangements severely disrupt polytene chromosome synapsis in the *dpp* region. In double rearrangement heterozygotes with similar breakpoints, sufficient synapsis occurs to allow for allelic complementation. The occurrence of complementation in these double-rearrangement heterozygotes demonstrates that these DTDs are not merely dominant enhancers of the heldout phenotype. If they were dominant enhancers, double-rearrangement genotypes should have been at least as heldout as the *DTD/+* individuals. Hence, for the DTDs of types *a* and *b*, I conclude that the disruption of transvection is mediated by disturbances in somatic chromosome pairing. In discussing the effects of these rearrangements, "phenotypic noncomplementation" and "synapsis-disruption" will be used interchangeably.

The pattern of rearrangements allows us to define two rules for synapsis-disruption of the *dpp* region of 2L. (*i*) Rearrangements with one break between 22F4 and 35D-E and the other in the proximal region of another chromosome arm disrupt synapsis and complementation. Thus, disruption can be due to a single break on 2L as far as 500 bands from *dpp*. However, the class *a* rearrangements with breakpoints in 32E to 35D-E are somewhat perplexing. While they obey rule *i*, they do not show restoration of complementation in double-rearrangement heterozygotes, even when the breakpoints of the double heterozygote are quite close and when they are both reattached to the same chromosome arm. We tentatively group the 22F4 to 32A and 32E to 35D-E rearrangements together, but we cannot rule out the possibility that the latter lesions are dominant enhancers of heldout. (*ii*) Rearrangements that have at least two breaks on 2L, one distal and one proximal to *dpp*, and that also result in *dpp* being medial or proximal, disrupt both synapsis and complementation. The only 2L break proximal to 22F (*dpp*) in these DTDs can be as distant as 40F. In general, the closer the distal and proximal 2L breakpoints are to *dpp*, the stronger the disruption of complementation.

The parallels between transvection at bithorax and at decapentaplegic are striking. In both systems, there has to be at least one break within a critical region and one outside of it. For bithorax, the critical region is 81F to 89D—the entire region of 3R proximal to bithorax (1). For *dpp*, the critical region appears to include 22F4 to 35D-E, as diagnosed by two-break rearrangements. Note, however, that there are three DTDs (two insertional translocations and one paracentric inversion) in which the only breakpoint proximal to *dpp* is in region 40. Thus, it may be that, when normal structure distal to *dpp* in these is disrupted, the critical proximal region on 2L is of larger extent—i.e., the entirety of 2L proximal to *dpp*. By comparison, the other well-documented instance of synapsis-dependent gene expression—the zeste–white system (2)—has a very short critical region, not extending out of section 3C (ref. 10; unpublished data).

Lewis (1) noted that bithorax transvection-disrupting rearrangements (BTDs) with breakpoints in the proximal portion of the bithorax critical region (from 81F to 85/86) always had quite distal breakpoints elsewhere in the genome. On the other hand, BTDs with breakpoints nearer to bithorax (86/87 to 89D) were recovered preferentially with more proximal breakpoints outside of the critical region. Interestingly, Lewis reported that a double BTD heterozygote with both breaks distal to 85 restored bithorax allelic complementation, whereas double BTDs with more proximal breaks remained mutant. This parallels the different behaviors of DTDs in 22F4 to 32A and 32E to 35D-E with regard to *dpp* complementation. For the *dpp* transvection effect, the rules appear to be similar to those for proximal BTDs affecting bithorax. For DTDs in the *dpp* system, breaks in the critical region (22F4 to 32A) are rejoined with proximal breaks elsewhere. This appears to be true, no matter what the distance between the 2L breakpoint and *dpp*.

Overall, it seems clear that rearrangements with a proximal breakpoint on one chromosome arm and a distal breakpoint on another are the simple rearrangements most effective in disrupting complementation, and by inference, disrupting normal somatic chromosome pairing as well. Indeed, in an independent experiment, we have identified a DTD in which a break in section 40 (the most proximal section of 2L) is reattached extremely distally to 100A (the tip of chromosome arm 3R).

The major component in initiating or maintaining somatic chromosome pairing in both systems appears to be located in regions of the chromosome arms proximal to the loci of interest. However, the apparently high frequency of recovery of insertional translocations as DTDs indicates that some pairing events can be initiated or stabilized by distal associations as well. Indeed, as stated above, the presence of the distal breakpoint in these insertional translocations appears to extend the interval of the proximal critical region on 2L, perhaps enlarging it to the entire chromosome arm.

Complementation can be restored in double heterozygotes, even when the DTDs reattach *dpp* to two different chromosome arms. This can be understood if there is a chromocentral organization in the nuclei of cells responsible for the heldout wing phenotype. It is striking that simple DTDs reattached to different chromosome arms are not equally disruptive to complementation (Fig. 2). These differences may well reflect a regular architectural feature of the chromocentral region in the nuclei responsible for conferring the heldout phenotype. For example, the chromosome arms may exit the chromocenter in a regular pattern, with the bases of 2L and 3L being closer than 2L and 4 (or 2R). This could facilitate correct pairing of distal 2L in 2L-3L translocations.

It is doubtful that all 57 *dpp* DTDs act by interfering with synapsis. A few of them (most likely the seven exceptional DTDs) actually may represent dominant enhancer mutations associated with one of each of their rearrangement breakpoints or induced simultaneously with them. Three of these exceptional rearrangements have a common breakpoint in 90A-B. Thus, there may be a locus in 90A-B that is capable of being mutated to a dominant enhancer of *dpp*. There are similar indications (data not shown) that 25D, 68F, and 70C may also contain such dominant enhancers. It is tempting to think that the one DTD not broken on 2L is a dominant enhancer because of a variegating position effect on the part of the 56F 5S rRNA gene cluster inserted into centric heterochromatin, which results in a generalized reduction in translational efficiency.

Interestingly, the two reported cases of synapsis-dependent allelic complementation—bithorax and decapentaplegic—involve putative multigene clusters. The bithorax locus clearly controls important spatial morphogenetic decisions; Lewis has presented evidence that the bithorax gene complex is organized in a manner colinear with the embryonic segments it controls (11). There is preliminary evidence that decapentaplegic controls a spatial decision within imaginal disks, and that the individual functions in this multigene cluster are organized colinearly with those disk geographic features that are under their control (6). Although these suggestions for decapentaplegic are tentative, they do point to common and unusual features of this locus and bithorax. Such features may be important in understanding why there are so few examples of transvection, even though a large number of loci are under intensive investigation.

Ashburner (12) has proposed a model involving propagative changes in chromatin structure to account for the synapsis dependence of certain chromosome puffing variants. This model could easily be applied to allelic complementation at bithorax and decapentaplegic. We would suppose that an early step in expression of functions within each cluster is a generalized decompaction of its chromatin superstructure. This relaxation of structure would be followed by other more specific regulatory events. Mutations exhibiting synapsis-dependent allelic complementation (such as dpp^4) could be interpreted as lesions that interfere with the initiation or propagation of the change in chromatin structure. Because of homologue synapsis in *Drosophila* (and other dipterans), these blocks to initiation or propagation can be circumvented through lateral interaction with a homologue that is wild type for that region of the cluster. Perhaps a unique structural feature of these loci (such as colinearity with the geographic organization of some tissues of the fly) reflects a property that makes them particularly sensitive to these sorts of propagative changes in chromatin structure. As an alternative, Judd (13) has invoked *trans* splicing of transcripts to explain transvection. Direct tests of such models should be feasible once recombinant DNA probes for these loci are available.

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1. Lewis, E. B. (1954) *Am. Nat.* **88**, 225–239.
2. Jack, J. W. & Judd, B. H. (1979) *Proc. Natl. Acad. Sci. USA* **76**, 1368–1372.
3. Ashburner, M. (1967) *Nature (London)* **214**, 1159–1160.
4. Korge, G. (1977) *Chromosoma (Berlin)* **62**, 155–174.
5. Lindsley, D. L. & Grell, E. H. (1968) *Genetic Variations of Drosophila melanogaster*, Carnegie Institution of Washington Publication no. 627 (Carnegie Inst., Washington, DC).
6. Spencer, F. A., Hoffman, F. M. & Gelbart, W. M. (1982) *Cell* **28**, 451–461.
7. Lifschytz, E. & Lindsley, D. L. (1972) *Proc. Natl. Acad. Sci. USA* **69**, 182–186.
8. Lindsley, D. L., Sandler, L., Baker, B., Carpenter, A. T. C., Denell, R. E., Hall, J. C., Jacobs, P. A., Miklos, G. L. G., Davis, B. K., Gethmann, R. C., Hardy, R. W., Hessler, A., Miller, S. M., Nozawa, H., Parry, D. M. & Gould-Somero, M. (1972) *Genetics* **71**, 157–184.
9. Wimber, D. E. & Steffensen, D. M. (1970) *Science* **170**, 639–641.
10. Gelbart, W. M. (1971) Dissertation (Univ. of Wisconsin, Madison, WI).
11. Lewis, E. B. (1978) *Nature (London)* **276**, 565–570.
12. Ashburner, M. (1977) in *Chromosomes Today*, eds. de la Chapelle, A. & Sorsa, V. (Elsevier/North-Holland, Amsterdam), Vol. 6, pp. 213–222.
13. Judd, B. H. (1979) in *Eucaryotic Gene Regulation*, ICN-UCLA Symposia on Molecular and Cell Biology, eds. Axel, R., Maniatis, T. & Fox, C. F. (Academic, New York), Vol. 14, pp. 107–115.