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Genetics

Drosophila melanogaster mutations suppressible by the suppressor of Hairy-wing are insertions of a 7.3-kilobase mobile element

(bithorax/cut/gypsy/scute/transposon)

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ABSTRACT **Certain spontaneous mutations of *Drosophila melanogaster* are suppressed by *su(Hw)*, the suppressor of Hairy-wing (3R-54.8). We find that mutations suppressible by *su(Hw)* result from insertions of a mobile element at the affected loci. The element, named gypsy, is approximately 7.3 kilobases long and includes 0.5-kilobase direct terminal repeats. It was first identified in DNA cloned from the bithorax chromosomal region of several *Drosophila* stocks carrying suppressible mutations of the bithorax complex. Cloned gypsy DNA was used as a probe to test for the association of gypsy with suppressible mutations at various other loci by hybridization *in situ*. Gypsy was found to be associated with 19 suppressible alleles at 10 different loci: yellow, Hairy-wing, scute, diminutive, cut, lozenge, forked, Beadex, hairy, and the bithorax complex. It was not found with wild-type or nonsuppressible mutations at any of these loci. Gypsy DNA was also used as a probe to clone the element and adjacent unique DNA from the loci of some suppressible mutations. This confirmed the presence of the full-length element and also provided cloned DNA from the previously uncloned loci scute and cut. The suppressor of Hairy-wing is generally recessive and behaves as a null mutation. Thus, the disruption of normal gene function caused by the inserted gypsy element appears to require some product of the wild-type suppressor gene, *su(Hw)*$^+$.**

The term "suppressor" was introduced into *Drosophila* genetics to denote a mutation that reverses the effects of a mutation in a gene located elsewhere, partially or completely restoring the wild phenotype. The earliest suppressors, including suppressor of sable and vermilion and suppressor of Hairy-wing, were at first misinterpreted as translocated chromosome segments containing the wild-type allele of the suppressed mutant (1–3). It eventually became clear, however, that these suppressors and several others are not duplications but instead are recessive mutations in specific suppressor genes (4–9).

Since these early studies, the genetics of *Drosophila* suppressors has received little attention (10). More is known, however, about the suppressor of Hairy-wing [*su(Hw)*;3R-54.8] than about the other suppressors in *D. melanogaster*. Lewis (11) reported tests for suppressibility by *su(Hw)* of 207 mutations at more than 123 loci, listing 15 mutations at 11 loci as suppressible. Remarkably, all the suppressible mutations arose spontaneously, even though about two-fifths of the mutations tested were induced, mainly by x-irradiation (12). The one seeming exception, sc^{D1}, is attributed to x-ray induction but may be the same as sc^{D2}, which is reported to be spontaneous. Both stocks were described by the same investigator and both are mutant at yellow, a very closely linked locus (12, 13).

The spontaneous origin of mutations suppressible by *su(Hw)* and their occurrence at dispersed sites suggested to one of us (M.M.) that these mutations are not simple sequence changes or rearrangements but instead result from the insertion of a mobile element at the affected locus. The element would then disrupt the normal function of the locus in flies wild-type for the suppressor. A decisive test of the presence of an inserted element became possible with the cloning of the bithorax region (unpublished data), where several suppressible mutations are known. We report here that suppressible alleles at bithorax and at various other loci are indeed each associated with the presence of a specific mobile element at the mutant locus.

MATERIALS AND METHODS

***Drosophila* Stocks.** Descriptions of mutants and balancers are given in Lindsley and Grell (12). Table 1 lists stocks used for *in situ* hybridizations to which specific reference is made.

Hybridization *in Situ*. Salivary chromosomes were prepared and hybridized as described (14) except that in some experiments the squashes were acetylated before NaOH denaturation (15), formamide was omitted, incubation was at 65°C for 4–6 hr, and hybridization mixtures contained 1 mM 5-iodocytidine and 0.2 mM 5-iodocytidine 5′-monophosphate.

Preparation and Screening of Recombinant Libraries. DNA was isolated from adult sc^1 ct^6 flies (14), partially digested with *Eco*RI, and fractionated on a sucrose gradient. Gradient fractions with fragments 10 kilobases (kb) or larger were pooled and precipitated with ethanol. DNA from the λ vector Sep 6 (16) was fully digested with *Eco*RI and *Sac* I to fragment the unwanted region and then was sedimented on a sucrose gradient. Fractions containing the vector arms were pooled and precipitated. Vector and fly DNAs (1 μg of each) were mixed and ligated with T4 ligase in a volume of 25 μl. Aliquots were packaged *in vitro* (17), and the phages were plated. DNA from the plaques was transferred to nitrocellulose filters (18), and the filters were hybridized with ^{32}P-labeled gypsy DNA. Positive plaques were replated at low density and rescreened, and single positive plaques were isolated and used to inoculate 25-ml bacterial cultures. After cell lysis, the phages were precipitated with polyethylene glycol. DNA was prepared from each of 25 such phage stocks by proteinase K digestion and phenol extraction. Aliquots were pooled in five groups of five, of which three groups were tested.

The DNA pools were nick-translated with ^{125}I-labeled dCTP and hybridized *in situ* to chromosomes of gt^1 w^a. With one group, which included the desired phages, the hybridizations were repeated with each individual phage stock. Stocks showing homology at the positions of scute or cut were amplified on plates and DNA was prepared for restriction mapping by formamide disruption (18).

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Abbreviation: kb, kilobase(s).

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Table 1. Stocks used for *in situ* hybridizations

Genotype	Source*
y Hw dm lz; su(Hw)^2/TM6 su(Hw)^f	E. H. Grell
sc cv ct^6 v; su(Hw)^{69k}/Ubx^{130}	E. H. Grell
sc cv ct^6 v; su(Hw)^{70a} e^s/Ubx^{130}	E. H. Grell
y sc^{D1}	Bowling Green
y sc^{D2}	Bowling Green
y^2	Bowling Green
y f	Caltech
y ct^K; bw	Caltech
w^{bf} f^5	Caltech
r^{sP1}/FM6	Caltech
r^{sP2}/FM6	Caltech
gt w^a	Caltech
f^{Kuhn}	David Kuhn

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Heteroduplex Analysis. To prepare heteroduplexes for electron microscopy, about 0.1 μl of each phage preparation in CsCl solution containing about 10 ng of DNA was added to 10 μl of 75% (vol/vol) formamide/0.25 M NaCl/0.1 M Tris/0.01 M EDTA, pH 8.5. The mixture was kept at 90°C for 30 sec and then at room temperature for 15–30 min. The mixture was diluted to 50 μl at a final composition of 55% formamide/0.05 M NaCl/0.06 M Tris/6 mM EDTA, pH 8.5, containing 20 μg of cytochrome *c* per ml and was spread onto a hypophase of 27% formamide/10 mM Tris/1 mM EDTA, pH 8.5 (19).

RESULTS

Several spontaneous alleles of the bithorax complex are among those suppressed by *su(Hw)*. DNA of bithorax has recently been isolated, and five of these suppressible alleles have been cloned. The mutations *bx^3*, *bx^{34e}*, *bxd^1*, *bxd^{55i}*, and *bxd^{Kuhn}* all have insertions of an identical 7.3-kb sequence named the gypsy element (unpublished data). A restriction map of the gypsy element, as found in *bx^{34e}*, is shown in Fig. 1.

For hybridization *in situ*, a recombinant phage (*bx^{34e}*–6a2) containing gypsy and 7 kb of unique DNA from the bithorax region was used initially as probe to detect homology to other copies of the gypsy element. Subsequent experiments used other phages isolated by homology to *bx^{34e}*–6a2 or used the 6.8-kb

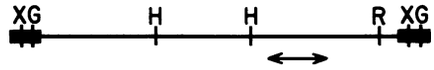

FIG. 1. Restriction map of gypsy mobile element in recombinant phage *bx^{34e}*-6a2. The element is approximately 7.3 kb long and has terminal direct repeats of approximately 0.5 kb (thicker lines). Each terminal repeat has sites for restriction enzymes *Xho* I and *Bgl* II. Gypsy has no sites for *Sal* I or *Bam*HI. Size marker represents 1 kb. R, *Eco*RI; H, *Hin*dIII; X, *Xho* I; G, *Bgl* II.

Xho I fragment from *bx^{34e}*–6a2 that includes almost all of the gypsy element (Fig. 1). ^{125}I-Labeled probe was hybridized to salivary gland chromosomes from mutant larvae. Most of the suppressible mutants tested are among those listed by Lewis (11, 20). All stocks showed grains over the chromocenter, but the sites of hybridization in the euchromatic arms varied in number and position from stock to stock. Such variation in the positions of hybridization between and even within stocks is typical of mobile elements in *Drosophila* (21–24). The average number of euchromatic sites for gypsy in the stocks tested was 5 (minimum, 0; maximum, 25; 30 stocks tested). Usually, only one or two larvae from each stock were tested.

The suppressible Hairy-wing mutation *Hw^1* is associated with a small duplication in chromosome subdivision 1B on the map of Bridges (25). *Hw* may affect the scute complex (26). It was tested in a stock homozygous for diminutive (*dm^1*) and lozenge (*lz^1*). Fig. 2*a* shows chromosomes of this stock hybridized *in situ* with gypsy. Four euchromatic sites are labeled, including the positions of Hairy-wing (1B), diminutive (3D), and lozenge (8D). Chromosomes from a larva with suppressible mutations at scute (*sc^1*) and cut (*ct^6*) showed hybridization at three sites, including subdivisions 1B and 7B, the locations of scute and cut, respectively (Fig. 2*b*). Larvae with the suppressible scute alleles *sc^{D1}* and *sc^{D2}* also showed grains at 1B and at one and three other sites, respectively. A larva with a second suppressible cut allele, *ct^K*, showed grains at 7B and four other sites. Three suppressible forked alleles were checked—*f^1*, *f^5*, and *f^{Kuhn}*. Larvae from all three stocks showed gypsy hybridization at 15F as expected (Fig. 2*c*) plus two, three, and four other sites, respectively. Likewise, a larva from a *y^2* stock showed three gypsy sites including 1A, the position of yellow (Fig. 2*d*).

There are two alleles of rudimentary, *r^{sP1}* and *r^{sP2}*, which are

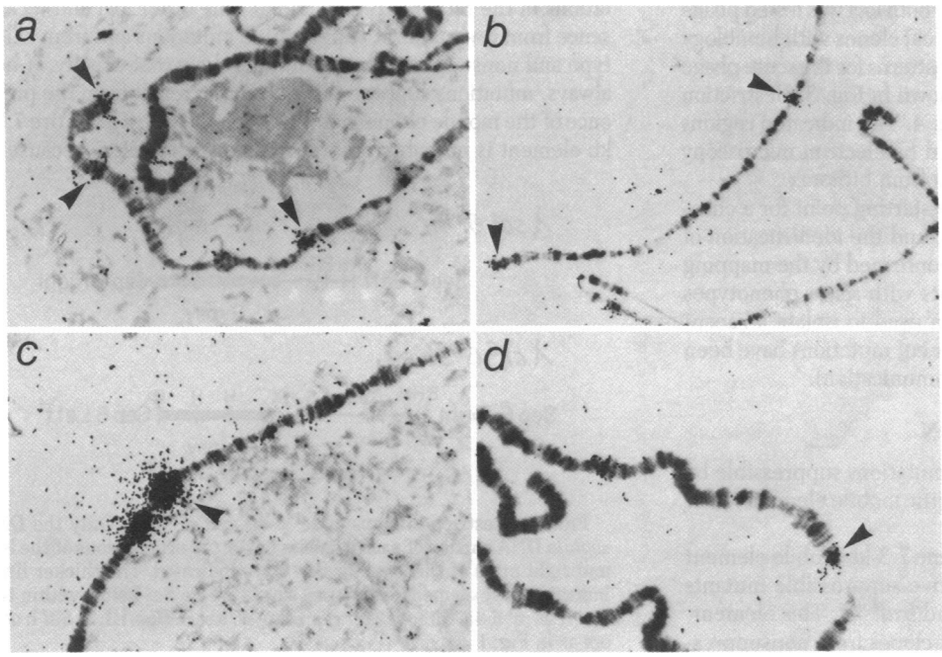

FIG. 2. Mutant chromosomes hybridized *in situ* with gypsy element probes. (*a*) Chromosomes of *y^1 Hw^1 dm^1 lz^1; su(Hw)^2/TM6 su(Hw)^f* male hybridized with 6.8-kb *Xho* I fragment of the gypsy element. Arrowheads mark the locations of Hairy-wing (1B), diminutive (3D), and lozenge (8D). (*b*) Chromosomes of *sc^1 cv^1 ct^6 y^1; su(Hw)^{70a} e^s/Ubx^{130}* hybridized with *bx^{34e}*–6a2. Arrowheads mark the locations of scute (1B) and cut (7B). (*c*) Chromosome of *w^{bf} f^5* hybridized with the *Xho* I fragment as in *a*. The arrowhead marks the location of forked (15F). This slide was exposed longer than the other three shown and accumulated more grains at the labeled sites. (*d*) Chromosomes of *y^2* hybridized with *ct^6* 6-3b. The arrowhead marks the position of yellow (1A). Grains also appear at 7B due to the single-copy DNA from the cut locus included in the probe (see Fig. 3*b*).

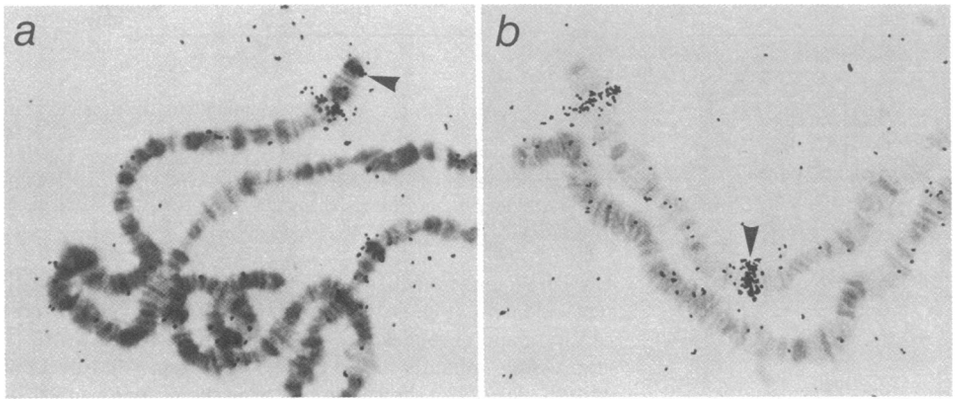

FIG. 3. Chromosomes of $gt^1\ w^a$ hybridized with clones from scute and cut. (*a*) Labeling with sc^1 6-4a. The arrowhead marks the location of scute (1B). (*b*) Labeling with ct^6 6-3b. The arrowhead marks the location of cut (7B).

partially suppressed by *su(Hw)* at 25°C but fully suppressed at 18°C (27). Neither of these stocks showed gypsy hybridization at the rudimentary locus (14D), although gypsy labeled three and two other sites, respectively.

We also checked the four available alleles of *su(Hw)* [($su(Hw)^2$, $su(Hw)^{69K}$, $su(Hw)^{70a}$, and $su(Hw)^f$)] for homology to gypsy. None had such homology at or near the location of *su(Hw)*, defined by $Df(3R)red^{P52}$ as 88B1-2 (20).

The presence of gypsy elements at suppressible mutant loci makes it possible to clone DNA from these loci by the method of transposon tagging (28). This approach is particularly useful for loci with gypsy mutations because there are relatively few gypsy insertions per genome that must be screened to find the one of interest. We used this method to clone fragments of the scute and cut loci. A genomic library was prepared with DNA from $sc^1\ ct^6$ flies and screened with a restriction fragment of the gypsy element. Clones from individual plaques homologous to gypsy were purified by replating, and DNA was prepared from each. DNA samples were pooled in groups of five clones each, and three groups were screened by hybridization *in situ*. Squashes were prepared from a *Drosophila* strain that had no gypsy element near scute or cut, so that we could test for the presence of unique DNA sequences from scute or cut adjacent to the gypsy DNA on the recombinant clones. We used a $gt^1\ w^a$ stock for the *in situ* tests; it had gypsy homology at 2B, 21D, 44D, and the chromocenter. All three groups included phages with homology in the region of cut at 7B, and one group also labeled scute at 1B. The group of five with homology to both loci was tested phage by phage, thereby identifying individual clones with homology to scute and cut. *In situ* hybridization patterns for the scute phage (6-4a) and the cut phage (6-3b) are shown in Fig. 3. Restriction maps of both clones are shown in Fig. 4. The indicated regions of homology to gypsy were confirmed by electron microscopy of DNA heteroduplexes with gypsies from bithorax.

The sc^1 6-4a clone was used as the starting point for a chromosomal walk within the scute locus, and the identification of the region as the scute complex was confirmed by the mapping of several rearrangement break points with scute phenotypes (14). The ct^6 6-3b clone has also been used to isolate adjacent DNA regions, and the lesions of other cut mutations have been located nearby (J. Jack, personal communication).

DISCUSSION

Two lines of investigation show that mutations suppressible by *su(Hw)* result from insertions of a specific mobile element at the affected loci.

First, in the bithorax region, the same 7.3-kb mobile element is found in cloned DNA of each of five suppressible mutants examined: bx^3, bx^{34e}, bxd^1, bxd^{55i}, and $bxd^{Kühn}$. This element, gypsy, has not been found in bithorax clones from nonsuppressible mutants or wild type. Like many other mobile elements, including some found in *Drosophila*, gypsy is bounded by terminal direct repeats. Examination of revertants of two suppressible mutations, bx^3 and bxd^1, shows that the full-length gypsy is no longer present but one copy of the 0.5-kb terminal repeat remains (unpublished data).

Second, as described here, cloned gypsy DNA hybridizes *in situ* at the cytological location of 12 suppressible mutations representing seven additional loci: *y*, *Hw*, *sc*, *dm*, *ct*, *lz*, and *f* (Table 2). Also, by using phage bx^{34e}–6a2 as probe for hybridization and cloning, gypsy has been found in the region of Beadex (17AC) in the suppressible mutant Bx^2 (W. Mattox and N. Davidson, personal communication) and in the region of hairy (66DE) in the suppressible mutant h^1 (R. Holmgren, personal communication). When no suppressible mutation is present we have seen no gypsy hybridization at the sites of any of these nine loci or in the bithorax region.

An exception to this otherwise complete association between suppressible mutation and the presence of gypsy occurs for two suppressible spontaneous rudimentary mutations, r^{sP1} and r^{sP2}, which showed no hybridization to gypsy DNA. Possibly their suppression does not involve gypsy. Alternatively, they may contain a functional portion of gypsy too divergent or too small to detect by our hybridizations. It is also possible that r^{sP1} and r^{sP2} are suppressed indirectly, by the effect of *su(Hw)* on some other locus at which gypsy is present.

In any case, the association of gypsy with suppressible mutations in the bithorax region and at nine other loci and its absence from revertants of suppressible mutations and from wild-type and nonsuppressible mutant loci show that usually, if not always, mutations suppressible by *su(Hw)* result from the presence of the mobile element at the affected locus. The entire 7.3-kb element is probably present in all or most cases, because it

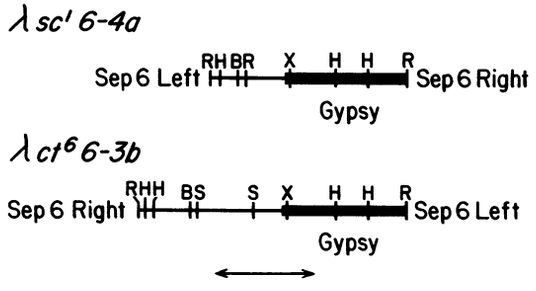

FIG. 4. Restriction maps of sc^1 6-4a and ct^6 6-3b. Only the *Drosophila* DNA portion of each clone is shown; the orientations of the left and right arms of the λ vector Sep 6 are indicated. The thicker lines indicate gypsy element sequences. There are no *Sal* I sites within the insert of sc^1 6-4a. Size marker represents 5 kb. B, *Bam*HI; S, *Sal* I; others as in Fig. 1.

Table 2. Mutations suppressible by suppressor of Hairy-wing

Locus	Allele	Hybridization *in situ*	Cloned	Comment*	Reference
yellow (1A)	y^2	+			11, 29
Hairy-wing (1B)	Hw^1	+		Mutation to Hw^2	11, 29
scute (1B)	sc^1	+	+		11
	sc^{D1}	+			11
	sc^{D2}	+			11
diminutive (3D)	dm^1	+			11
cut (7B)	ct^6	+	+	Reversion	11, 29
	ct^K	+		Suppression by $su(Hw)^2/+$	31
lozenge (8D)	lz^1	+			11
rudimentary (15A)	r^{sP1}	−		ts suppression	27
	r^{sP2}	−		ts suppression	27
forked (15F)	f^1	+		Reversion, mutation to f^{3N}	11
	f^5	+			†
	f^{Kuhn}	+		Suppression by $su(Hw)^2/+$	‡
Bar (16A)	B				11, 29
Beadex (17AC)	Bx^2	+	+		11, §
hairy (66DE)	h^1	+	+		¶
bithorax (89E)	bx^3		+	Reversion, gypsy excision	11, 30
	bx^{34e}		+	Partial reversion	11
	bxd^1		+	Reversion, gypsy excision	11, 30
	bxd^{51j}				20
	bxd^{55i}		+		20
	bxd^{Kuhn}		+		‡
cubitus interruptus (101F-102A)	ci^1				11

* ts, temperature-sensitive. Reports of instability of the suppressible allele are noted.
† Partially suppressed by homozygous $su(Hw)^2$ (E. B. Lewis, personal communication).
‡ D. Kuhn, personal communication.
§ Gypsy cloned by W. Mattox and N. Davidson (personal communication).
¶ Suppression discovered and gypsy cloned by R. Holmgren (personal communication).

is found in every one of the nine suppressible mutations that have been cloned (Table 2).

There is considerable indication that, relative to other spontaneous mutants, those suppressible by *su(Hw)* occur preferentially at certain loci. In the bithorax region, it is remarkable that most of the spontaneous mutations listed by Lewis (11, 20), five of eight, are suppressible. In contrast, at the white locus, where the greatest number of spontaneous mutations has been tested, none of 12 such mutations is suppressible (11, 12). Indeed, the proportion of suppressible mutations among spontaneous mutations at all loci in Lewis' compilation is only about 10%. Aside from the bithorax region, multiple occurrences of suppressible mutation are known at scute, cut, and forked, where eight of nine tested spontaneous mutations are suppressible (12) (Table 2), again suggesting that suppressible mutations occur preferentially at certain loci. Most of the loci at which suppressible mutations have been found are known to be complex, although, considering the case of the white locus, complexity may not be the only determinant. The observed preferences could reflect locus specificity in the occurrence of gypsy or in the proportion of insertions with mutant effect. It may also be that gypsy mutations are suppressible at some loci but not at others. Within a locus, suppressible mutations can be widely spaced. The mutations ct^6 and ct^K are 0.16 centimorgan apart, probably corresponding to more than 50 kb (31). There are also lesser, although still considerable, distances between the two *bx* gypsy insertions and among the three *bxd* insertions (unpublished data).

The expression of mutant phenotype by suppressible alleles appears to require a product of the wild-type suppressor gene, $su(Hw)^+$. In the absence of this product, function is restored—that is, the mutation is suppressed. This follows from the fact that the suppression of mutations by *su(Hw)* is generally recessive. Little if any suppression is seen if even one copy of the wild-type allele $su(Hw)^+$ is present. Exceptions occur with ct^K and f^{Kuhn}, which are suppressed by $su(Hw)^2/su(Hw)^+$. This may be an effect of dosage of the $su(Hw)^+$ product, one dose not being sufficient to obtain the full mutant effect of gypsy in these cases. Indeed, the ct^K example has provided additional evidence that *su(Hw)* is effectively nonfunctional. The mutation ct^K is suppressed as well by the heterozygous deficiency for *su(Hw)*, $Df(3)red^{P52}/su(Hw)^+$, as by $su(Hw)^2/su(Hw)^+$, indicating that $su(Hw)^2$ is equivalent to a null mutation (20).

The recessiveness of *su(Hw)* and its behavior as a null mutation rule out any mechanism of suppression in which the suppressor gene produces a suppressor tRNA, such as occurs in the case of translational nonsense suppression well documented in other organisms. Indeed, any mechanism of translational suppression of insertion mutations within coding regions seems unlikely. It may also be noted that no tRNA hybridization is seen at 88B, the location of *su(Hw)* (32). In the separate case of suppressor of sable, *su(s)*, there is evidence that suppression affects RNA modification (32) and enzyme inactivation (33). Nevertheless, the mechanism of suppression has not been fully established for this or any other *Drosophila* suppressor system.

The germ-line excision of gypsy that occurs in the reversion of suppressible alleles might be taken as suggesting that suppression by *su(Hw)* results from excision of gypsy in somatic cells. Any such excision, however, must be limited or specific to certain tissues. Otherwise, we would not have detected gypsy hybridization *in situ* at the locations of Hairy-wing, diminutive, and lozenge in the suppressed stock $y^1\ Hw^1\ dm^1\ lz^1$; $su(Hw)^2/su(Hw)^f$ from which the squash of Fig. 2*a* was prepared. Moreover, there is no evidence for mosaic expression of suppressed alleles as might result from variable excision. Considering the limited evidence, somatic excision, although not ruled out, does not appear to be the basis of suppression by *su(Hw)*.

Of the numerous suppressor systems known in other organisms, that which appears to have the most detailed similarity to *su(Hw)* is the suppression of certain insertion mutations at the *his4* locus of the yeast *Saccharomyces cerevisiae*, a system which has also been likened to the *Spm* system of maize (34–36). Insertions of the 5.6-kb mobile element Ty1 upstream of the *his4* mRNA initiation site cause mutations that are *his*$^-$ in a wild-type background but are suppressed by mutations in unlinked genes. Other *his4* mutations such as frame-shifts and nonsense are not affected—that is, suppression is specific for the Ty1 insertion mutations. Reversions occur at relatively high frequency and the most common of these have lost Ty1 but retain one copy of the Ty1 0.25-kb terminal repeat sequence. The mechanisms responsible for the mutant effect of the insertions and for their suppression are not known, but the location of the insertions upstream from the mRNA initiation site suggests an effect on the control of transcription rather than on subsequent steps in gene expression. The mutant effect of the insertions may result from disruption of a region whose integrity is required for normal transcriptional control. Suppressor mutations might then act by allowing a promoter in the mobile element to direct transcription of the mutant gene (37). This, however, leaves unexplained why the long terminal repeat remaining in revertants does not similarly disrupt gene expression and why, in *Drosophila*, suppressible gypsy mutations at a given locus can be widely separated. In these *Drosophila* and yeast systems, therefore, it may be that the effect of the intact mobile element extends over a considerable distance, possibly by altering the local DNA or chromatin structure and that this alteration is reduced or prevented in suppressed strains.

Regardless of what mechanisms are involved, we might ask why the wild-type gene *su(Hw)*$^+$ is maintained, even though its presence causes gypsy insertions to disrupt gene function. One possibility is that *su(Hw)*$^+$ would be adaptive even in the absence of gypsy. In this sense, the interaction of *su(Hw)*$^+$ and gypsy would be fortuitous. An alternative possibility is that *su(Hw)*$^+$ prevents some deleterious manifestation of the mobile element. Considering the wide occurrence and profound genetic effects of endogenous mobile genetic elements and retroviruses, it seems likely that stable genes would have evolved to control their activity. On this view, *su(Hw)*$^+$ and, perhaps, the wild-type alleles of other suppressor genes may protect the organism against mobile elements by reducing their mobility or interfering with some other aspect of their expression. In doing so, however, the expression of the locus at the site of insertion might also be disrupted. Suppression might then activate the mobile element as well as the mutated locus.

In addition to *su(Hw)*, there are several other *D. melanogaster* suppressors known to affect mutations at more than one locus or to suppress some mutations but not others at a given locus (12). These include *su(s)* [1-0], *su(w*^{a}*)* [1-0.1], *e(w*^{e}*)* [1-32], *su(f)* [1-65.9], and *su(pr)*[3R-95.5]. Like *su(Hw)*, all are recessive. Although not many suppressible mutations are known, they are all spontaneous and some are known to be unstable. There appear to be specific interactions between these different systems of suppression, as indicated by the suppression of lz^1, f^1, and f^5 and the enhancement of w^a by *su(f)*; the suppression of lz^1 and f^1 by $e(w^e)$; the suppression of pr^1 and the enhancement of lz^1, bx^3, and bx^{34e} by *su(s)*; and the enhancement of Hw^1 by *su(pr)* (12; E. B. Lewis, personal communication; W. Gelbart, personal communication). In the case of $su(w^a)$, there is evidence that a mobile element is involved: the suppressible mutation w^a results from insertion of the 5-kb element copia (28). Thus, there may be several possibly interacting systems of suppression similar to the system of *su(Hw)*, all involving suppressor genes that affect the expression of mutant loci where mobile elements are present.

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