INTERACTIONS BETWEEN *WHITE* GENES CARRIED BY A LARGE TRANSPOSING ELEMENT AND THE *ZESTE*[1] ALLELE IN *DROSOPHILA MELANOGASTER*

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ABSTRACT

TE146, a large transposing element of *Drosophila melanogaster*, carries two copies of the *white* and *roughest* genes in tandem. In consequence, z^1 w^{11E4}; *TE146(Z)*/+ flies have a zeste (lemon-yellow) eye color. However, one in 10^3 *TE146* chromosomes mutates to a red-eyed form. The majority of these "spontaneous red" (*SR*) derivatives of *TE146* have only one copy of the *white* gene and are, cytologically, two- to three-banded elements, rather than six-banded as their progenitor. The *SR* forms of *TE146* are also unstable and give zeste-colored forms with a frequency of about one in 10^4. One such "spontaneous zeste" (*SZ*) derivative carries duplicated *white* genes as an inverted, rather than a tandem, repeat. The genetic instability of this inverted repeat form of *TE146* is different from that of the original tandem repeat form. In particular, the inverted repeat form frequently produces derivatives with internal rearrangements of the *TE* and gives a much lower frequency of *SR* forms. In addition, two novel features of the interaction between w^+ alleles in a *zeste* background have been found. First, copies of w^+ can become insensitive to suppression by *zeste* even when paired. Second, an inversion breakpoint may disrupt the pairing between two adjacent w^+ alleles, necessary for their suppression by *zeste*, without physically separating them.

A large transposing element (*TE*) from *Drosophila melanogaster* that carries alleles of two genes, *white* and *roughest*, has been described by ISING (ISING and RAMEL 1971, 1976; ISING and BLOCK 1981, 1984). This *TE* is unstable; it may be lost (ISING and BLOCK 1981; GUBB *et al.* 1984, 1985), may transpose to a new chromosome location (ISING and BLOCK 1981) or may undergo internal rearrangements (ISING and BLOCK 1981; GUBB *et al.* 1984). The interaction between the *white* gene(s) of the *TE* and the *zeste* mutation is a sensitive assay for internal rearrangements of the *TE*. This is because the suppression of *white* by *zeste* depends not only on the presence of two copies of *white* (GANS 1953) but also on their physical proximity (GREEN 1967; GELBART 1971; JACK and JUDD 1979; GREEN 1984).

Members of ISING's family of *TE*s fall into three classes according to their interaction with the *zeste*[1] (z^1) allele (G. ISING, personal communication). The majority give red eyes when heterozygous in a z^1 w^{11E4} background and lemon-

TABLE 1

Description of chromosomes

Chromosome	Cytology
Df(2L)A72, b cn bw	*Df(2L)35B1.2;35B7*
Df(2L)A178, b rd^s pr cn	*Df(2L)35B1.2*
Df(2L)A446, b cn bw	*Df(2L)35B1.2;35E1.2*
Df(2L)fn2, pr cn	*Df(2L)35A3;35B2-4*
Df(2L)fn3, pr cn	*Df(2L)35B1;35B3-4*
Df(2L)b81a1, Adh^{uf3} cn	*Df(2L)34D3;35B1*
In(2LR)Sco^{R+1}, l(2)br29^{ScoR+1}	In(2LR)35D1.2;44C3-5
b l(2)br3^{AR2} pr	Normal
l(2)br22^{FT1} Adh^{n11} cn	Normal
b el^2 Adh^F	Normal
z^1 w^{11E4}	Normal
y^2 z^1 Dp(1;1)w^{+R}	See text
b TE36(R) pr pk cn sp	See text
b TE146(Z)	See text
al dp b TE146(Z) pr l(2)pwn cn	See text
In(2LR)0, Cy dp^{iv1} Adh^{nB} pr cn^2 (= Cy0, Adh^{nB})	
In(1)w$^-$ rst$^-$, y; In(2L)Cy + In(2R)Cy dp cn^2 TE (w^a rst$^+$) In(1)3C;20	

yellow (*i.e.*, zeste) eyes when homozygous. An example of this class of *TE* is *TE36* (GUBB *et al.* 1984). By this criterion they carry a single functional copy of *white*. Some *TE*s, however, give a zeste eye color even when heterozygous in a z^1 w^{11E4} background. ISING and BLOCK (1981) suggested that these *TE*s carry two functional copies of *white*. The third class of *TE* does not give zeste eyes even when homozygous in a z^1 w^{11E4} background. These may be mutant in the proximal region of *w*, required for the interaction of this gene with *zeste* (GREEN 1959).

G. ISING (personal communication) has documented examples of a *TE* which can change between red- and zeste-eyed forms in a z^1 w^{11E4} background. This suggests that these *TE*s may undergo both duplication (*i.e.*, red → zeste) and partial loss (*i.e.*, zeste → red). In this paper, spontaneous derivatives of *TE*146(*Z*) that can be recovered on the basis of the interaction between this *TE* and *zeste* will be described.

MATERIALS AND METHODS

Stocks: The chromosomes used in this study are listed in Table 1. The *TE* chromosomes have been described by GUBB *et al.* (1984, 1985). The z^1 w^{11E4} chromosome is z^1 w^{11E4} of GANS (1953). The w^{11E4} allele is a deletion (ZACHAR and BINGHAM 1982). The z^1 *Dp(1;1)*w^{+R} chromosome was derived by unequal exchange between w^a and w^{a4} and carries a duplication of the proximal part of *white* (GREEN 1963; GOLDBERG, PARO and GEHRING 1982). Males carrying this chromosome have the lemon-yellow eye color typical of z^1 w^+/z^1 w^+ females.

Loci of the Alcohol dehydrogenase genetic region used in this study are *elbow* (*el*), *lethal(2)br22* (*l(2)br22*), *lethal(2)br29* (*l(2)br29*), *no-ocelli* (*noc*), *outspread* (*osp*), *Scutoid* (*Sco*)

and *Alcohol dehydrogenase* (*Adh*). The genetic characteristics of these loci are described by WOODRUFF and ASHBURNER (1979) and ASHBURNER, TSUBOTA and WOODRUFF (1982). With the exception of *lethal(2)pawn* (*l(2)pwn*), used to ensure that *TE146* chromosomes remain heterozygous when balanced over *CyO*, all other mutations are described in LINDSLEY and GRELL (1968).

The *al dp b TE146(Z) pr l(2)pwn cn* stock used in the experiments to be described (and those of GUBB *et al.* 1985) was derived from a single male that was a double recombinant between *al dp b TE146(Z)* (from G. ISING) and *pr l(2)pwn cn sp* chromosomes. This male was mated to *w; b TE36(R) pr pk cn sp/CyO, Adh^{nB}* females to give a *w; al dp b TE146(Z) pr l(2)pwn cn/CyO, Adh^{nB}* stock (used for the spontaneous *TE* loss experiments of GUBB *et al.* 1985), whose *X* chromosome was replaced with z^1 w^{11E4} by crossing a single male to z^1 w^{11E4} females. Thus, all *TE146(Z)* derivatives are from a common *TE146(Z)* second chromosome.

Crosses: Crosses were set up in 1 × 4 inch vials or in 200 ml bottles on yeast-glucose food. All crosses were grown at 25°. Complementation crosses were scored from the 10th to the 18th day after setting up.

In the *TE146-SR* experiments, 30 pairs of z^1 w^{11E4}; *TE146(Z)/CyO, Adh^{nB}* parents were set up per bottle and were transferred every 3 days for a period of 9 days. Bottles were coded so that clusters of exceptional progeny from the same parents would be recognized. The parental flies were carefully checked to ensure that they were all zeste eyed. The *TE146-SZ* experiments were set up in the same way, the parental flies being checked to ensure that all were red eyed.

The bristle phenotypes of *Sco* heterozygotes were scored by counting the number of major dorsal head and dorsal thoracic bristles [see table 4 of ASHBURNER *et al.* (1983) for sites scored] of ten males and ten females per genotype.

Cytology and *in situ* hybridization: For cytological analysis of polytene chromosomes, temporary propionic-orcein-carmine squash preparations of larval salivary gland chromosomes were made by the usual procedures and were interpreted with the aid of the revised polytene chromosome maps (see LEFEVRE 1976). The procedure for *in situ* hybridization of tritium-labeled probes to salivary gland polytene chromosomes has been described previously (GUBB *et al.* 1984). The probes used are described by GUBB *et al.* (1985).

Nomenclature: The original form of *TE146* will be called *TE146(Z)*, indicating its phenotype when heterozygous in a z^1 w^{11E4} background. Derivatives will be named according to their origin [*i.e.*, spontaneous (*S*) or gamma-ray-induced (*G*)], and phenotype in a z^1 w^{11E4} background [*i.e.*, red (*R*), zeste (lemon yellow) (*Z*), white (*W*) or variegating (*V*)]. The progenitor chromosome will be indicated within the parentheses immediately before the stock designation. For example, *TE146(Z:SR100:SZ4)GW500* would indicate gamma-ray-induced white derivative number 500 of *TE146(Z:SR100)SZ4*, itself spontaneous zeste derivative number 4 of *TE146(Z)SR100*, which was spontaneous red derivative number 100 of the original *TE146(Z)* form. The accession numbers are uniquely assigned, so that stock names can be abbreviated. Thus, *TE146-GW500* would be the shortened form of *TE146(Z:SR100:SZ4)GW500*, although abbreviations of the form *GW500* can (and will) be used when there is no possibility of ambiguity. We shall use the abbreviation *TE146* as a generic shorthand for *TE146(Z)* and all of its derivatives.

RESULTS

Preliminary: *TE146(Z)* is an insertion into chromosome arm *2L*, just proximal to bands 35B1.2. This insertion causes a strong mutant phenotype of the *no-ocelli* (*noc*) gene. The cytology and elementary genetics of *TE146(Z)* have been described in detail by GUBB *et al.* (1985). The eye color of z^1 w^{11E4}; *TE146(Z)/+* is zeste in both males and females. An identical eye color is seen

in flies of the following genotypes: *y z Dp(1;1)w*$^{+R}$/Y; +/+, *y z Dp(1;1)w*$^{+R}$; *TE146(Z)*/+, *y z Dp(1;1)w*$^{+R}$; *TE146(Z)/TE146(Z)* and z^1 w^{11E4}; *TE146(Z)/TE146(Z)*. If *TE146(Z)* carried only one functional copy of *white*, the eye colors of z^1 w^{11E4}; *TE146*/+ and *y z Dp(1;1)w*$^{+R}$; *TE146(Z)*/+ would be red, not zeste. This is because single, unpaired copies of *white* are not suppressed by *zeste* (GANS 1953; GELBART 1971; JACK and JUDD 1979). These data suggest that *TE146(Z)* carries at least two functional copies of w^+. *In situ* hybridization with a clone containing homology to *w* shows two distinct bands of silver grains within *TE146(Z)* (GUBB *et al.* 1985).

There are two other *TE*s that map near to *TE146*, *TE94* in 34C4.5 (M. ASHBURNER, unpublished results) and *TE36* in 35B9-35C1 (GUBB *et al.* 1984). Both give red eyes, when heterozygous with a wild-type chromosome, in a z^1 w^{11E4} genetic background. *TE36* gives zeste eyes when homozygous on z^1 w^{11E4} background (GUBB *et al.* 1984), but the phenotype of homozygous *TE94* is not known (this chromosome carries a lethal mutation, *l(2)br38*, which maps at the same cytological location as *TE94*). Heterozygotes between *TE146(Z)* and *TE36(R)* are zeste (on z^1 w^{11E4}), heterozygotes between *TE146(Z)* and *TE94* are red eyed (on z^1 w^{11E4}). This suggests that a *trans* interaction can occur between adjacent *TE*s over at least seven polytene chromosome bands, although perhaps not over 27 bands (see DISCUSSION). Unlinked *TE*s, for example *TE77* (on chromosome arm *3R* at 89E), do, as expected, suppress *zeste* when both *TE*s are heterozygous. Thus, both z^1 w^{11E4}; *TE146(Z)*/+; *TE77*/+ and z^1 w^{11E4}; *TE77*/+ flies are red eyed, although z^1 w^{11E4}; *TE77/TE77* flies are zeste in eye color. These data confirm previous results with other insertional translocations of *white* (GELBART 1971; JACK and JUDD 1979; GELBART and WU 1982; GREEN 1984).

Spontaneous red-eyed derivatives of *TE146(Z)*: Spontaneous red-eyed flies were recovered from a stock of z^1 w^{11E4}; *al dp b TE146(Z) pr l(2)pwn cn/CyO*, *Adh*^{nB}. Twenty-four independent red-eyed flies were recovered in 41,958 progeny (one in 1,748). The occurrence of clusters of red-eyed progeny indicates that they may be premeiotic events (see Table 9). There is cytological evidence of genetic identity between flies recovered as cluster-sibs. In addition to the main series of *TE146(Z)SR* derivatives (numbered *SR1* to *SR68*), five others (*SR100* to *SR104*) have been analyzed.

The majority of *TE146(Z)SR*s are deleted forms of *TE146(Z)*, showing two to three, rather than six, bands in polytene chromosome preparations (Figure 1 and Table 2). Cytologically, two groups of two- to three-band *SR*s can be distinguished. In one group the bands of the *TE* are very close together (Figure 1a), whereas in the other they are more widely separated (Figure 1b and c).

Two of the *SR*s are cytologically exceptional. One, *TE146(Z)SR14*, is associated with a pericentric inversion with one breakpoint within the *TE*, In(2LR)35B1·2;42F1·2-43B1·2 (Figure 1d). A crossover between this inversion and *In(2LR)Sco*$^{R+1}$ (= In(2LR)35D1·2; 44C3-5)—that is, *In(2LR)Sco*$^{R+1L}$*TE146(Z)SR14*^{R}—is *rst*$^+$ but w^-. This result shows that *In(2LR)TE146(Z)SR14* is broken within the *TE*, and it indicates that the progenitor *TE146(Z)* chromosome carried a copy of *rst*$^+$ proximal to all of its

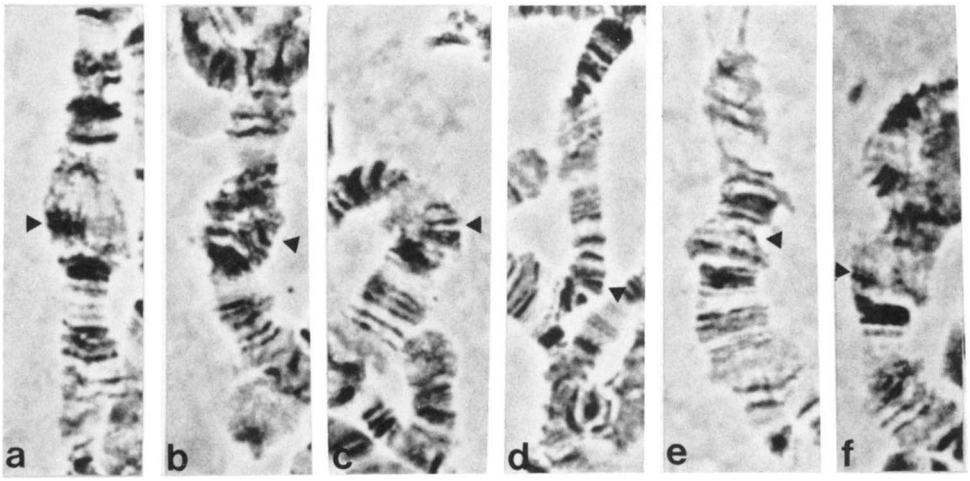

FIGURE 1.—The polytene chromosomes of *SR* derivatives of *TE146(Z)*. All heterozygous with *CyO*, Adh^{nB}. a, A "close-banded" form (*SR45*). b and c, Two "open-banded" forms (*SR22* and *SR24*). d, *In(2LR)TE146(Z)SR14*, asynapsed homologue showing the 42F/35B junction (arrow). The bracketed bands are probably *TE* derived. e, The very small *TE* associated with *Df(2L)TE146(Z)SR48*. f, The small *TE* associated with *Df(2L)TE146(Z)SR54*. Photographs of *TE146(Z)* itself were published in GUBB *et al.* (1985). In fact, the cytological appearance of *TE146(Z)* is indistinguishable from that of *TE146(Z:SR100)SZ3* shown in Figure 4g.

copies of w^+. *SR14* and *SR15* were recovered as a cluster and are cytologically identical. The second exceptional *SR*, *TE146(Z)SR48*, shows only a trace of an insertion in 35B (Figure 1e). Its cluster-sib (*SR53*) was cytologically identical. Since both the *SR14* and *SR48* types of derivative are rare, the cytological identity of their cluster-sibs confirms that members of a cluster may be derived from a single genetic event.

The original form of *TE146(Z)* carries w^+, rst^+ and is associated with an amorphic allele of *noc*. Despite being viable when homozygous or when hemizygous with noc^- deletions, *TE146(Z)* is almost lethal with $l(2)br29^{ScoR+1}$ (GUBB *et al.* 1984). *TE146(Z)* also enhances the expression of *Sco*, *TE146(Z)/Sco* heterozygotes having only about 16 dorsal head and thoracic bristles per fly instead of the 25–27 bristles per fly of *+/Sco* (ASHBURNER *et al.* 1983). At least one member of each cluster of the *TE146(Z)SR*s has been characterized with respect to these genetic interactions (Table 3). With two exceptions, they are very similar to the original form of the *TE*.

The exceptions are *SR48* (and its cluster-sib *SR53*) and *SR54*. Both are deletions, both of the *TE* and of adjacent chromosome material. *SR48* is, cytologically, a very small insertion (Figure 1e), and *SR54* is a two-band insertion (Figure 1f). The extent of the deletions of chromosome *2* material associated with these derivatives can be seen from the data presented in Tables 3 and 4. In both, the deletion extends from the *TE* proximally to uncover both *osp* and *Adh* (Figure 2). Neither uncovers *l(2)br3* (proximal to *Adh*), nor *l(2)br22* (distal to *l(2)br29*). [*l(2)br29* is now regarded as a lethal function of the *noc* gene (see CHIA *et al.* 1985a).]

TABLE 2

Eye-color phenotypes and cytology of *SR* derivatives of *TE146(Z)*

SR	*SR/TE36(R)*	*SR/TE146(Z)*	Pigment[a]	Cytology	
				No. of bands	Position[b]
SR2	z	z	0.318	2–3	c
SR3	z/+ v	z	0.321	3	s
SR14	dz	z	0.804	In(2LR)35B;42F1.2-43B1.2	
SR24	dz	z	0.369	3	s
SR25	z	z	0.291	2	c
SR33	dz	z	0.279	3	s
SR35	z	z	0.340	2–3	c
SR38	z	z	0.361	3	s
SR43	z	z	0.385	3	c
SR44	dz	dz	0.360	3	c
SR46	dz	z		3	c
SR47	z	z	0.265	3	c
SR48	z	z	0.235	1	
SR51	z	z	0.362	2–3	c
SR54	z	z	0.281	2	
SR60	z	z	0.349	3	c
SR64	z	z	0.342	3	s
SR68	dz	z	0.255	4	s
SR100	dz	z	0.283	2–4	?
SR102	dz	dz	0.307	2	c
SR22	z/+ v	z/+ v	0.784	2	s
SR23	+	+	0.827	3–4	s
SR36	+	+	0.780	5–6	s
SR41	z/+ v	z/+ v	0.758	4	s
SR45	+	+	0.702	3	c
SR103	+	+	0.696	6[c]	c
SR104	+	+	0.646	3	c
TE146(Z)	z	z	0.781	6	s

Key to eye-color phenotypes: + = red; z = zeste; bw = brownish; z/+ v = variegating for zeste and red; dz = dark zeste.

[a] Eye pigments of males measured as in GUBB *et al.* (1984). All pigment assays were done on flies of the genotype w^1;*b TE146 pr*/+.

[b] Position of bands: c = close together; s = spaced apart; see text and Figure 1.

[c] Also *TE301*, see text and Figure 3d.

Both *Df(2L)TE146(Z)SR48* and *SR54* retain one copy of w^+ and at least one of rst^+, indicating that there is one copy of *w* and at least one copy of *rst* distal to the second copy of *w* on the original *TE*. With the evidence from the breakpoint of *SR14*, these data are most simply interpreted to mean that the original *TE146(Z)* is a tandem duplication with the distal-proximal order w^+ rst^+ w^+ rst^+ or an inverted duplication with the order rst^+ w^+ w^+ rst^+ (Figure 2). The cytology of *TE146-SZ1* (see below) suggests that the w^+ rst^+ w^+ rst^+ order is more likely for *TE146(Z)* itself.

In a series of experiments to recover red derivatives of *TE146(Z)* after irradiation (D. GUBB, J. ROOTE, A. WILKINS, AND M. ASHBURNER, unpublished

TABLE 3

The genetic characteristics of *TE146(Z)* and its spontaneous red (*SR*) derivatives

			Bristle count of *Sco/TE146*					
TE146	*ScoR+1*	*Sco*	Mean	SE	*fn2*	*fn3*	*noc*	*rst*$^{-a}$
TE146(Z)	16/10317	660/2758	16.30	0.59	150/560	987/3223	noc	
SR2	3/203	67/268	15.90	0.63	61/194	57/142	noc	81/380
SR3	2/245	69/237	15.00	0.44	61/219	126/413	noc	62/283
SR14	1/185	68/282	15.00	0.53	60/138	67/156	noc	59/282
SR22	0/254	83/204	16.95	0.52	56/158	66/188	noc	68/285
SR23	1/128	45/204	14.85	0.49	67/191	57/181	noc	79/307
SR24	0/163	55/202	15.00	0.49	75/194	52/162	noc	70/246
SR25	4/254	78/339	13.30	0.69	72/216	144/291	noc	45/194
SR33	0/224	76/330	12.55	0.39	75/266	101/268	noc	42/195
SR35	0/260	43/251	13.15	0.52	54/216	34/112	noc	30/187
SR36	1/286	45/187	13.85	0.61	89/251	48/129	noc	39/105
SR38	2/216	74/271	15.40	0.44	90/207	55/155	noc	37/181
SR41	3/151	69/161	17.20	0.46	57/186	77/338	noc	45/205
SR43	2/134	52/225	14.50	0.52	84/212	67/164	noc	66/266
SR44	1/345	39/203	13.95	0.48	128/297	141/523	noc	47/272
SR45	2/262	47/186	14.90	0.57	69/177	52/130	noc	54/324
SR46	0/148	44/146	14.20	0.44	50/197	57/150	noc	27/162
SR47	9/231	67/254	15.85	0.50	69/258	34/104	noc	74/329
SR48	9/233	54/168	16.00	0.40	26/904	24/203	noc	36/264
SR51	0/195	62/274	15.60	0.38	65/230	50/110	noc	81/308
SR54	1/239	54/218	16.30	0.46	15/380	32/396	noc	82/417
SR60	3/199	67/239	14.65	0.60	59/219	64/123	noc	53/221
SR64	0/141	59/238	13.70	0.45	85/237	95/323	noc	72/280
SR68	0/149	26/150	14.90	0.91	43/113	98/304	noc	31/147
SR100	4/250	50/210	14.00	0.51	63/155	142/245	noc	86/352
SR103	0/114	141/653	16.05	0.48	65/619	54/216	noc	45/191
SR104	0/150	119/623	15.80	0.54	46/164	91/286	noc	50/247

The numbers of Cy^+ progeny, over the total numbers of progeny, from crosses between *TE146/CyO*, *Adh*^{nB} and *l(2)br29*$^{ScoR+1}$*/CyO*, *Sco/Cy Bl*, *Df(2L)fn2/CyO* and *Df(2L)fn3/CyO* are shown. The noc phenotype was scored in heterozygotes with the two deletions (*fn2* and *fn3*). The *rst* data show relative viabilities of *rst*$^-$/Y; *TE146/+* males. SE = standard error.

[a] All wild type for *roughest*. *TE146(Z)* is also *rst*$^+$ (GUBB *et al.* 1985).

results), several dominant suppressors of *zeste* that segregated from *TE146* were recovered. No unlinked *Su(z)*s were found in the spontaneous red experiments, but five of the *SR*s (*SR23*, *SR36*, *SR45*, *SR103* and *SR104*) are unusual in that they are red eyed (in a z^1 w^{11E4} background) even when heterozygous with the original *TE146(Z)*. Two other *SR*s (*SR22* and *SR41*) variegate for zeste and red in z^1 w^{11E4}; *TE146(Z)/TE146(Z)SR* genotypes (Table 2). The majority of *SR*s do not affect the suppression of *w* by *zeste* when heterozygous with the original form, *TE146(Z)*. There are several possible explanations for the exceptional *SR*s that act as dominant suppressors of *zeste*. For example, they may carry a linked dominant suppressor of *zeste*, which could be either within the *TE* or at a locus similar to one of those characterized by others (GREEN 1967; GELBART 1971; KALISCH and RASMUSON 1974; PERSSON 1976; WU 1984).

TABLE 4

The genetic characteristics of two *TE146(Z)SR*s that are deletions

Chromosome	*SR48*	*SR54*
Df(2L)A72	59/205[a]	54/274[a]
Df(2L)A178	46/218[b]	62/203[b]
Df(2L)A446	52/443[b]	1/328[b]
Df(2L)b81a1	74/332[b]	55/220[b]
osp	osp	osp
ADH[c]	null	null
l(2)br22^{FT1}	48/145	48/198
l(2)br3^{AR2}	64/132	84/140

The numbers of Cy^+ progeny, over the total numbers of progeny, from crosses between stocks with the tester chromosomes balanced over *CyO*, *Adh*^{nB} are given.

[a] Phenotypically outspread.

[b] Phenotypically outspread and noc.

[c] ADH assays were histochemical spot tests of *SR/Adh*^{n2} genotypes, performed by the method of O'DONNELL *et al.* (1975).

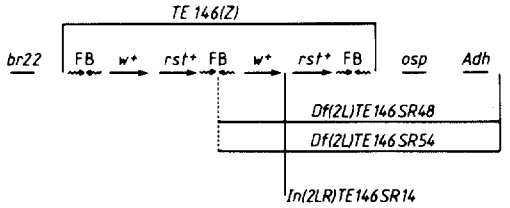

FIGURE 2.—A possible model for the organization of *white* and *FB* sequences in *TE146(Z)*. See text for discussion of *FB* sites. The relative positions of the *w* and *rst* genes are based on the inferred breakpoints of *In(2LR)TE146(Z)SR14*, *Df(2L)TE146(Z)SR48* and *Df(2L)TE146(Z)SR54*. There is no evidence that *SR14* is not broken within the proximal copy of w^+. Similarly, the *SR48* and *SR54* breakpoints could be in the central *FB* site or within the proximal copy of w^+. With respect to the centromere, this diagram is orientated in the conventional direction, *i.e.*, the telomere of chromosome arm *2L* is to the left, and the centromere of chromosome *2* is to the right.

Alternatively, a third copy of *white*, at a sufficient distance from *TE146* that no w^+-w^+ interaction occurs, would also behave as a dominant suppressor of *zeste*. To distinguish between these hypotheses, females homozygous for z^1 w^{11E4} on their *X* chromosomes and heterozygous for a *b SR pr* (? *Su(z)*) chromosome were backcrossed to z^1 w^{11E4}/Y; *b pr sple/CyO*, *Adh*^{nB} males. Nonrecombinant Cy^+ progeny will be either white eyed (z^1 w^{11E4}; +/*b pr sple*) or black with purple eyes (z^1 w^{11E4}; *b SR pr/b pr sple*). Crossovers between *b* and the *SR* are expected at a frequency of about 0.9% and will be either white eyed and black bodied or will have a purple eye color. If the eye phenotype of the *SR* is due to a linked *Su(z)*, then this may be separable from the intact *TE146* by exchange. For example, a *Su(z)* mapping distal to *b* or proximal to *pr* will give zeste-eyed progeny (*e.g.*, z^1 w^{11E4}; *b TE146 pr/b pr sple*) and their reciprocal class (*e.g.*, z^1 w^{11E4}; *Su(z)/b pr sple*). It should be pointed out that *pr* does not affect the zeste eye color phenotype of z^1 w^{11E4}; *TE146*.

Recombinants were made from the following chromosomes: *SR23* (n = 593

Cy^+ progeny), *SR36* (n = 641), *SR45* (n = 536), *SR103* (n = 293) and *SR104* (n = 486). All except *SR103* behaved as if the dominant suppression of *zeste* was inseparable from the *SR* itself. The frequency of exchange between *b* and the *SR*s varied between 0.34 and 0.90% in the different experiments. For *SR103*, however, there were 11 wild-type and 12 zeste-black progeny, showing that the *SR103* chromosome carries an extra copy of w^+ 7.86% to the left of the original *TE*.

These data were confirmed for *SR23*, *SR36* and *SR103* by *in situ* hybridization of their polytene chromosomes with a cloned *w* gene fragment (Figure 3). For *SR23* and *SR36* the only autosomal sites of hybridization were at 35B; each showed two sites of *w* homology within the *TE*. With *SR103* the original *TE* at 35B showed two sites of *w* homology, but in addition, there was a third site at 31AB (Figure 3c). This *TE* is cytologically visible as two bands between 31A8 and 31B6 in the polytene chromosomes (see Figure 3d). *SR103*, therefore, represents a transposition of *half* of the original *TE146*(*Z*), giving a single "unpaired" copy of w^+ unsuppressible by *zeste* (to be called *TE301*). The structure of the *SR103* chromosome is, therefore, *TE301*(*R*) *TE146*(*Z*). There is no *FB* site at 31AB in the original *TE146*(*Z*) chromosome.

Most heterozygotes between *TE146*(*Z*)*SR*s and *TE36*(*R*) (on z^1 w^{11E4}) are zeste in phenotype, although sometimes the eye color is a bit darker than is normal for zeste. There are five exceptions that give red eyes when heterozygous with *TE36*(*R*) on z^1 w^{11E4}. These chromosomes, *SR23*, *SR36*, *SR45*, *SR103* and *SR104*, also give red eyes when heterozygous with *TE146*(*Z*). Heterozygotes with the two *SR*s that variegate with *TE146*(*Z*) (*SR22* and *SR41*) also variegate with *TE36*(*R*) (Table 2). These data confirm that these *SR*s carry a *white* allele unsuppressible by *zeste*.

Presumably these exceptional *SR*s carry at least one *w* allele that is unable to be suppressed by *zeste* despite being adjacent to another copy of *w*. This mutant *white* allele must be functional, otherwise z^1 w^{11E4}; *SR/TE146*(*Z*) flies would be *zeste*. There is a dramatic difference in pigment levels between those *SR*s whose w^+ gene(s) cannot be suppressed by *zeste* and those that can. Males of all the *SR*s that are red eyed (or variegate for red on a *zeste* background) when heterozygous with *TE146*(*Z*) have the same amount of extractable eye pigment as *TE146*(*Z*) itself (Table 2). The males of those *SR*s that are zeste eyed when heterozygous with *TE146*(*Z*) have approximately half as much eye pigment as *TE146*(*Z*) males (Table 2). There is only one exception to this rule, *SR14*. This *SR* is the only one that is associated with a chromosome aberration (an inversion). When heterozygous with *TE146*(*Z*), it is phenotypically zeste, but *SR14* has approximately the same amount of extractable eye pigment as *TE146*(*Z*) itself.

These data are consistent with the conclusion that the majority of *SR*s have only one functional copy of the *white* gene, but that those *SR*s whose *w* gene(s) cannot be suppressed by z^1 have two. The exceptional example, *SR14*, will be discussed below.

From red to zeste forms of *TE146*: Spontaneous zeste-eyed flies were recovered from different *TE146*(*SR*)s (Table 5). *TE146-SZ1*, *SZ2*, *SZ7–SZ10*,

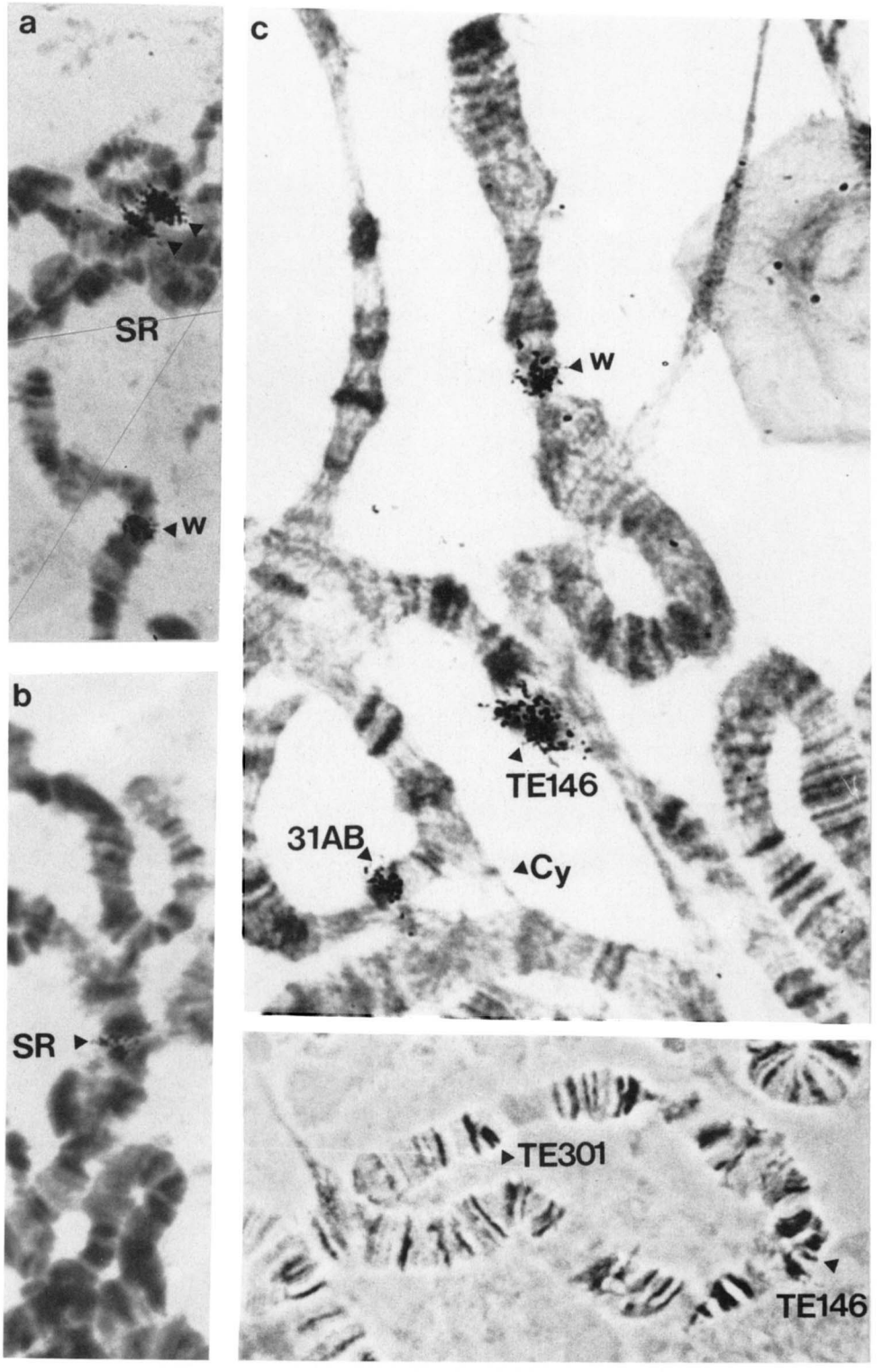
a
SR
w
b
SR
c
w
TE146
31AB
Cy
TE301
TE146

TABLE 5

Origin and genetic properties of spontaneous zeste (*SZ*) derivatives of *TE146(Z)SRs*

				Bristle count of *Sco/SZ*					
SZ	Origin	*ScoR+1*	*Sco*	Mean	SE	*fn2*	*fn3*	*noc*	*rst*$^{-a}$
SZ1	*SR100*	2/176	79/252	14.75	0.47	47/105	94/290	noc	28/135
SZ3	*SR100*	1/184	155/452	17.90	0.83	73/272	85/211	noc	33/105
SZ18	*SR100*	0/191	61/202	17.75	0.76	43/133	87/228	noc	26/158
SZ6	*SR23*	6/280	98/316	15.60	0.98	67/169	164/360	noc	33/124
SZ13	*SR23*	0/178	53/156	16.30	0.44	39/135	61/203	noc	61/296
SZ14	*SR23*	1/331	44/188	17.35	0.32	49/216	112/376	noc	76/403
SZ16	*SR23*	6/328	51/159	17.70	0.47	37/155	183/568	noc	86/368
SZ4	*SR36*	2/249	48/169	14.50	0.67	127/432	75/201	noc	65/243
SZ7	*SR36*	0/219	79/285	14.90	0.80	55/215	49/127	noc	45/162
SZ8	*SR36*	1/178	74/265	18.15	0.59	57/207	140/319	noc	36/176
SZ9	*SR36*	0/118	90/310	17.40	0.71	75/301	75/221	noc	36/192
SZ10	*SR36*	1/152	60/226	17.20	0.56	41/199	84/289	noc	63/221

The numbers of Cy^+ progeny, over the total numbers of progeny, from crosses between *SZ/CyO*, Adh^{nB} and $l(2)br29^{ScoR+1}/CyO$, *Sco/Cy Bl*, *Df(2L)fn2/CyO* and *Df(2L)fn3/CyO* are shown. The noc phenotype was scored in heterozygotes with the two deletions (*fn2* and *fn3*). The *rst* data show relative viabilities of rst^-/Y; *SZ*/+ males. SE = standard error.

[a] All survivors phenotypically rst^+.

SZ13, *SZ14* and *SZ16* were from screens, and *TE146-SZ3*, *SZ4*, *SZ6* and *SZ18* were found in *SR* stock bottles.

Three screens for *SZ*s were done. The first, with *TE146(Z)SR100* gave one *SZ* event in 18,110 flies. The second, with *TE146(Z)SR23*, gave three *SZ*s in 6,894 flies and the third, with *TE146(Z)SR36*, gave four *SZ*s in 7,921 flies. The frequency of *SZ*s was lower for *SR100* than for either *SR23* or *SR36*. *SR23* and *SR36* differ from *SR100* in that they remain red eyed when heterozygous with *TE146(Z)* and *TE36(R)* (Table 2). The genetic and cytological properties of these *SZ*s are summarized in Tables 5 and 6. With respect to their genetic interactions with mutations in the *noc* region, all resemble *TE146(Z)*.

Two *SZ* derivatives of *SR100*, *SZ1* and *SZ3* have duplicated the bands of *TE146(Z)SR100* (*SZ2* was a cluster-sib of *SZ1* and appears to be identical to it); however, they are quite different in their cytology. *SZ3* looks like the parental

FIGURE 3.—*In situ* hybridization of spontaneous red derivatives of *TE146(Z)* with a probe (M365 of GOLDBERG, PARO and GEHRING 1982) to the *white* gene [see GUBB *et al.* (1985) for methods]. a, *SR36*, an unusual *SR* that acts as a dominant *Su(z)*, with two copies of *w* within the *TE* (arrows); the normal, *X*-linked copy of *white* is also indicated (w). The *TE* chromosome is heterozygous with *CyO*, Adh^{nB} but asynapsed in region 35. b, *SR27*, a *SR* with only one copy of *w* within the *TE*. c, The *SR103* chromosome with the original *TE146(Z)* at 35B, with two copies of *w* and the new *TE301* at 31AB with one copy (see text). The normal *X*-linked copy of *white* is also indicated (w). The *TE* chromosome is heterozygous with *CyO*, Adh^{nB}; Cy indicates the proximal breakpoint of *In(2L)Cy* in 34A. d, The polytene chromosomes of *SR103* showing a six-band *TE* at 35B (*TE146(Z)*) and the new two-band *TE*, *TE301*, between 31A8 and 31B6. (The small, silver grain size in Figure 3b is due to the use of Ilford L4 emulsion, rather than Ilford K2 as in the other preparations.)

TABLE 6

The eye-color phenotypes of spontaneous zeste derivatives of *TE146(Z)SRs* when heterozygous with *TE146(Z)* and *TE36(R)* and their cytological descriptions

			Cytology	
SZ	*TE146(Z)*	*TE36(R)*	No. of bands	Repeat[a]
SZ1	z/+ v	z	6	rr
SZ3	z	z	6	tr
SZ18	z	z	4–6	tr
SZ6	z	z	6	tr
SZ13	z	z	6	tr
SZ14	z	z	6	tr
SZ16	z	z	6	tr
SZ4	z	z	In(2LR)35B;42F1.2-43B1.2	
SZ7	z	z	6	tr
SZ8	z	z	6	tr
SZ9	z	z	6	tr
SZ10	z	z	4–6	tr

Key to eye-color phenotypes: z/+ v = variegating for zeste and red; z = zeste.

[a] rr = inverted repeat; tr = tandem repeat.

TE146(Z) with six polytene chromosome bands (Figure 4g), but *SZ1* is clearly an inverted duplication (Figure 4b and c). In polytene chromosomes, *SZ1* appears as a blunt ending "side arm" from the chromosome axis at 35B1.3. This side arm has three to four bands and results from intrahomologue synapsis between a three-band inverted repeat of the form ABCCBA. Both *SZ1* and *SZ3* give a typical zeste phenotype when heterozygous in a z^1 w^{11E4} background.

The cytological appearance of *SZ1* is constant and quite distinct from the original *TE146(Z)*. The bands of *SZ1* are often rather fuzzy ("heterochromatic") (Figure 4c). The *SZ1* chromosome has not been studied cytologically in homozygous larvae, because the chromosome is semilethal, even after the removal of *l(2)pwn* by exchange. However, a spontaneous derivative of *SZ1*, *TE146(Z:SR100:SZ1)SV201* is homozygous viable, and its polytene chromosomes have been studied. When heterozygous, the *SV201* chromosome is very similar to *SZ1* (Figure 4d). When homozygous, the *SV201* chromosome forms a rather homogeneously staining block in 35B (Figure 4e). The chromosomes are very wide at the site of the *TE*, as would be expected were there two side arms. Occasionally, two well-banded side arms are visible; the cytological appearance of homozygous *SV201* then resembles that of the 2B region of the *X* chromosome (Figure 4f).

SZ4 arose in a stock of *TE146(Z)SR36*. *SR36* is, itself, an unusual *SR* in two respects: heterozygotes between *SR36* and either *TE146(Z)* or *TE36(R)* are red eyed (on z^1 w^{11E4}), and cytologically, *SR36* is a large, 5- to 6-banded element.

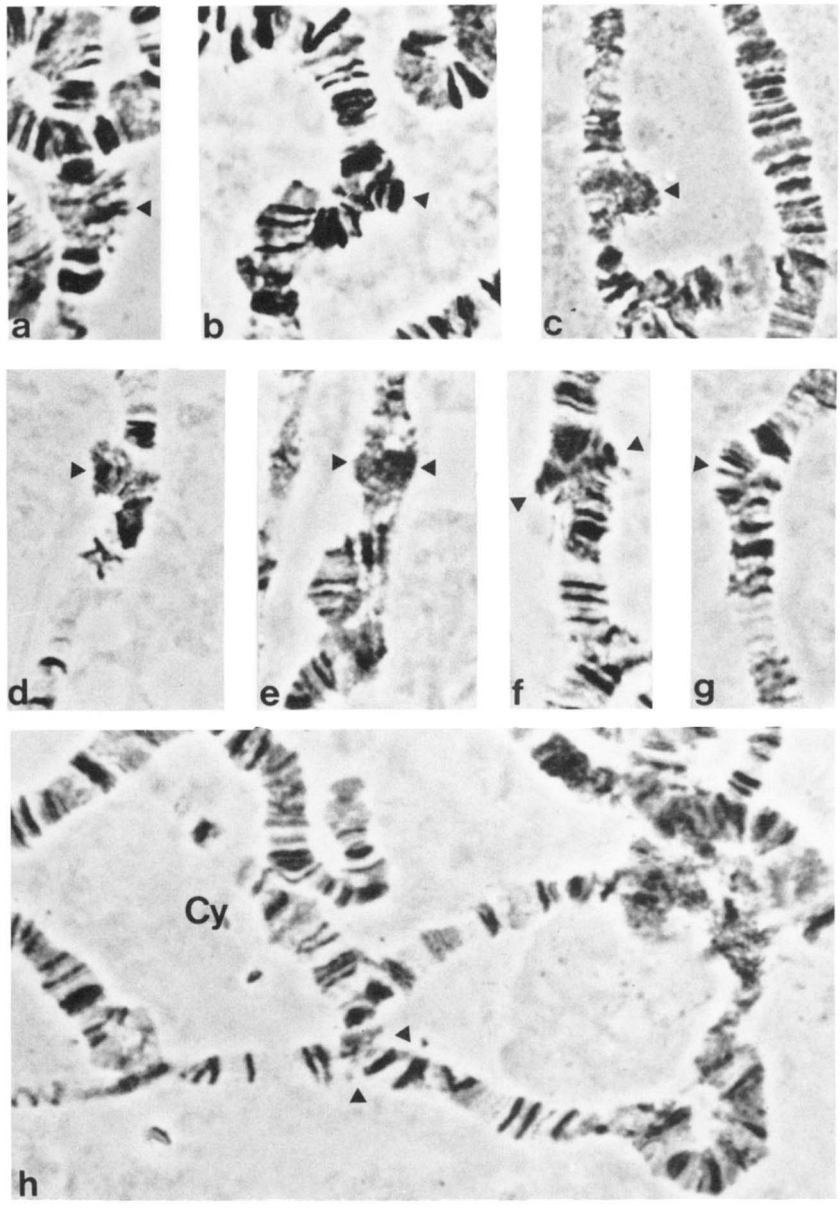

FIGURE 4.—The polytene chromosomes of *SZ* derivatives of *TE146(Z)SR*s. a, *TE146(Z)SR100/+*, the progenitor to *SZ1* and *SZ3*. b and c, The inverted repeat form of *TE146(Z:SR100)SZ1/+* showing relatively "banded" (b) and relatively "heterochromatic" (c) forms of this *TE*. d, *TE146(Z:SR100:SZ1)SV201/+*, a cytologically similar derivative of *SZ1*. e and f, *TE146(Z:SR100:SZ1)SV201* homozygotes in relatively "heterochromatic" (e) and relatively "banded" (f) forms. g, The tandem repeat *TE146(Z:SR100)SZ3/+*. h, The inversion associated with *SZ4*, *In(2LR)TE146(Z:SR36)SZ4/CyO*, Adh^{nB}; the 42F-43B/35B breakpoint of the inversion is indicated by the arrow (compare with Figure 1d), and Cy indicates the left break of *In(2L)Cy*.

SZ4 was a spontaneous zeste-eyed derivative of *SR36*. Remarkably, the *SZ4* chromosome carries a pericentric inversion with breakpoints similar to those of the pericentric inversion associated with *SR14*, *i.e.*, In(2LR)36B1.2;42F1.2-43B1.2 (Figure 4h). The presence of *TE*-derived bands near the breakpoints of *SR14* and *SZ4* introduces some uncertainty as to the precise bands, on chromosome arm *2R*, at which these inversions are broken. Genetically, these breakpoints differ because *In(2LR)TE146(Z:SR36)SZ4* is associated with an amorphic mutation of *prickle* (*pk*) (but not of the closely linked gene, *spiny-legs*). These genes have been localized to the region between 42E3 and 43C3 (M. ASHBURNER, in GUBB and GARCIA-BELLIDO 1982). Neither *In(2LR)TE146(Z)SR14* nor the progenitor of *SZ4*, *i.e.*, *TE146(Z)SR36*, are mutant for *prickle*. A recombinant between *SZ4* and *SR14*, *In(2LR)SR14^{L}SZ4^{R}* has been synthesized and is also *pk*$^{-}$. Since both *SR14* and *SZ4* carry *l(2)pwn*, it is not possible to test genetically for the deletion of 42F1.2 to 43B1.2, because all available deletions that include *pk* also include *l(2)pwn*. Other spontaneous zeste derivatives of *SR36* are cytologically unchanged, although small rearrangements within the *TE* might not be visible.

Further derivatives of *TE146(Z:SR100)SZ1*: *SZ1*, the inverted repeat form of *TE146*, was studied to see if its stability was similar to that of the original tandem repeat, *TE146(Z)*. Two white-eyed clusters and six red-eyed clusters were found in 61,305 progeny. The spontaneous loss frequency of *SZ1* is, therefore, somewhat less than that of *TE146(Z)* (one in 30,000, compared to one in 22,000). The frequency of red-eyed derivatives is, however, much lower (one in 10,217, compared to one in 1,748). The proportion of the red derivatives of *SZ1* that remain red eyed even when heterozygous with *TE146(Z)* (on z^1 w^{11E4}) is higher than for the *SR* derivatives of *TE146(Z)* (see Tables 2 and 8). Four of the *SR* derivatives of *SZ1* are dominant suppressors of *zeste*; that is, they are red eyed when heterozygous with *TE146(Z)* on a z^1 w^{11E4} background. Attempts to separate the *TE* and the "*Su(z)*" by recombination have failed in all cases (*SR200* 407 *Cy*$^{+}$ flies scored; *SR203* n = 704 *Cy*$^{+}$; *SR206* n = 1059 *Cy*$^{+}$; *SR208* n = 201 *Cy*$^{+}$). As with the *SR* derivatives of *TE146(Z)*, there is a good correlation between the dominant suppression of *zeste* by the *SR200* series and their pigment levels. All of the *SR200*s that suppress *zeste*, in z^1 w^{11E4}; *TE146(Z)/SR* flies, have approximately the same amount of extractable pigment as *TE146(Z)* or *TE146-SZ1* heterozygotes. All those that are suppressible by *zeste* have approximately half as much pigment (Table 8).

Four other derivatives of *SZ1* were found in stock bottles (*SW204*, *SW205*, *SR204* and *SV201*). *TE146(Z:SR100:SZ1)SR201* gave rise to both white (*SW*) and variegating (*SV*) (red on zeste) progeny the first generation after its isolation (subsequently it has appeared to be relatively stable).

The genetic properties of these derivatives of *SZ1* are summarized in Tables 7 and 8. The two *SV*s, five of the seven *SR* derivatives of *SZ1* and *SR209*, a spontaneous red derivative of *SR100-SZ6*, remain genetically very similar to *TE146(Z)* and *TE146-SZ1* themselves. The remaining two *SR*s, *SR204* and *SR205*, do not. These chromosomes retain a cytologically visible insertion at

TABLE 7

The genetic properties of spontaneous white (*SW*), red (*SR*) and variegating (*SV*) derivatives of *TE146(Z:SR100)SZ1*

			Bristle count of *Sco/TE146*					
S	*ScoR+1*	*Sco*	Mean	SE	*fn2*	*fn3*	*noc*	*rst*$^-$
SW200	0/172	110/281	15.00	0.46	84/234	114/245	noc	8/151
SW201	94/282	258/709	26.25	1.18	58/157	64/167	noc$^+$	(rst)
SW202[a]	3/185	30/170	14.55	0.72	51/104	56/160	noc	2/160
SW204	0/161	50/232	14.70	0.58	123/417	88/298	noc	(rst)
SW205	2/166	53/247	16.05	0.68	67/255	187/547	noc	6/271 (rst) 2/243 (rst) 7/695 (rst)
SR200	0/212	134/534	14.10	0.70	70/241	54/164	noc	41/158 (+)
SR201	0/187	97/331	13.90	0.69	36/135	56/189	noc	44/189 (+)
SR203	0/149	49/195	14.30	0.40	67/230	117/321	noc	43/189 (+)
SR204	90/300	87/294	23.16	0.54	64/149	245/818	noc[b]	53/269 (+)
SR205	89/279	109/274	22.90	0.45	62/162	200/577	noc[b]	45/158 (+)
SR206	0/157	86/433	16.20	1.18	40/164	76/265	noc	38/193 (+)
SR208	0/196	57/173	16.05	0.36	80/169	121/385	noc	74/276 (+)
SR209[a]	2/150	87/314	16.50	0.43	55/148	86/240	noc	31/163 (+)
SV200[a]	0/148	91/290	13.40	0.67	103/267	71/228	noc	64/224 (+)
SV201	0/146	55/320	13.90	0.72	54/191	74/303	noc	45/197 (+)

The number of Cy^+ progeny, over the total numbers of progeny, from crosses between *TE146/CyO, Adh*^{nB} and *l(2)br29*$^{ScoR+1}$*/CyO, Sco/Cy Bl, Df(2L)fn2/CyO* and *Df(2L)fn3/CyO* are shown. The noc phenotype was scored in heterozygotes with the two deletions. The *rst* data show relative viabilities of *rst*$^-$/Y; *TE146/+* males. SE = standard error.

[a] *SW202* and *SV200* are both derived from *TE146(Z:SR100:SZ1)SR201* and not from *TE146(Z:SR100)SZ1*. *SR209* was derived from *TE146(Z:SR23)SZ6*. *SV201, SR204, SW204* and *SW205* were found in a stock of *TE146(Z:SR100)SZ1* that was *l(2)pwn*$^+$ and could, therefore, have been derived from *SZ1* homozygotes. All other *SZ1* derivatives were from a *TE146(Z:SR100)SZ1 l(2)pwn* chromosome balanced over *CyO, Adh*^{nB}.

[b] The noc phenotypes of *SR204* and *SR205*, when heterozygous with the *noc*$^-$ deletion *Df(2L)fn3*, are much weaker than those of other *SR*s.

35B1.2 (Table 8). However, they are relatively weak alleles of *noc*, are not strong dominant enhancers of *Sco* and are viable with *l(2)br29*$^{ScoR+1}$.

The white derivatives differ. One (*SW201*) is similar to the spontaneous white derivatives of *TE146(Z)* itself in being *noc*$^+$, *w*$^-$, *rst*$^-$, viable with *l(2)br29*$^{ScoR+1}$ and not a dominant enhancer of *Sco* (see GUBB *et al.* 1985; Table 7). However, the others are quite different from the *TE146(Z)SW*s. They remain strong *noc* alleles, are lethal with *l(2)br29*$^{ScoR+1}$ and enhance *Sco*. They are all *rst*$^-$ as well as *w*$^-$.

Cytologically, the *SZ1* derivatives are bizarre. *SZ1* itself is an inverted repeat form of *TE146*. One of its white derivatives (*SW200*) is a two- to three-banded element, similar to the common class of *TE146(Z)SR*s (Figure 5a and b). Yet, it differs genetically from the *SR*s in being *w*$^-$ and *rst*$^-$. *SW201* is viable with

TABLE 8

The eye-color phenotypes of *SZ1* derivatives in z^1 w^{11E4} background and their cytology

				Cytology	
	TE146(Z)	TE36(R)	Pigment[a]	No. of bands	Repeat[b]
SW200	z	+		2–3	
SW201	z	+		0	
SW202	z	+		?4	<rr
SW204	z	+		2	<rr
SW205	z	+		2	<rr
SR201	z	bw	0.305	5–6	<rr ?
SR204	z	dz	0.417	2–4	not rr
SR205	z	z	0.362	2–4	
SR209	z	z	0.364	2–4	
SR200	+	bw	0.781	5–6	rr (like *SZ1*)
SR203	+	+	0.712	5–6	<rr
SR206	+	+	0.933	5–6	
SR208	+	+[c]	0.781	2–4	
SV200	z^d	z^d		6–8	rr
SV201	z^d	z^c		6–8	rr
TE146—SZ1	z	z	0.731	6	rr

For eye-color phenotypes, see footnote to Table 2.
[a] Eye pigments of males determined as in GUBB *et al.* (1984).
[b] rr = inverted repeat; <rr = internal deletion of inverted repeat.
[c] Males, Moire-like; females, purplish.
[d] Red crescent at posterior edge of eye.

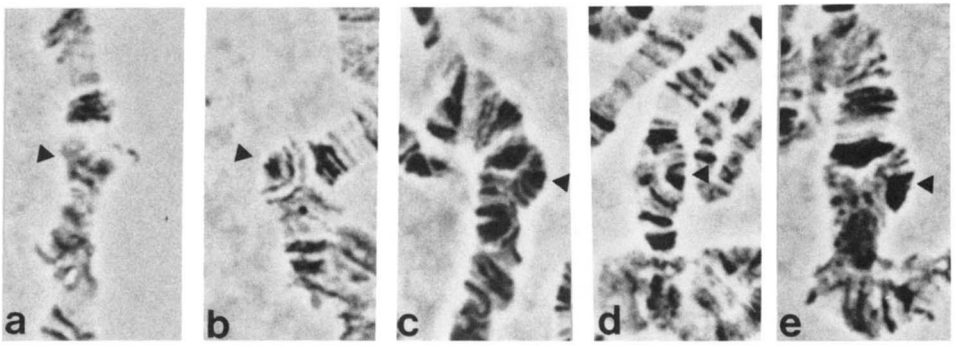

FIGURE 5.—Derivatives of *TE146(Z:SR100)SZ1*. a, *SW201*, a complete loss of cytologically visible material; b, *SW202*, showing remnant bands in region 35B (arrow); c, *SR201*; d, *SR202*; and e, *SV200* (all heterozygous with *CyO*, Adh^{nB}). See text for further explanation.

l(2)br29^{ScoR+1}, fails to enhance *Sco* and is phenotypically noc$^+$; cytologically it lacks any sign of an insertion in chromosome *2* (Figure 5a). The three other *SW* derivatives (*i.e.*, *SW202*, *SW204* and *SW205*) are quite different from these; cytologically they appear as if they are internal deletions of *SZ1*. The outer bands of these three derivatives pair within the *TE*, but the inner ones do not (Figure 5b). Thus, in complete contrast to all *SW* derivatives of *TE146*(Z), most

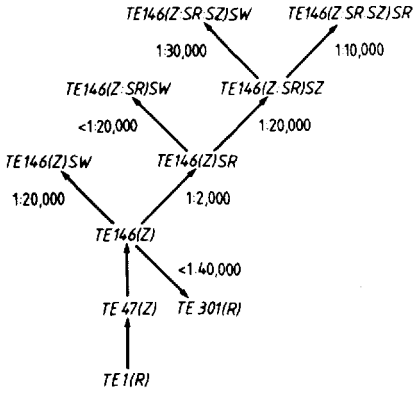

FIGURE 6.—The origins of the different derivatives of *TE146(Z)* showing the approximate spontaneous frequencies of each class of event (where known). (See Table 9 for details.) The frequencies given for *TE146(Z)SR* and *TE146(Z:SR)SZ* are for *TE146(Z)SR100* and *TE146(Z:SR100)SZ1*, respectively.

of those of *SZ1* retain several bands, despite being functionally deleted for the *TE*s *white* and *roughest* genes.

The *SR* derivatives of *SZ1* are also heterogeneous (Figures 4c and d). Four of them (*SR204*, *SR205*, *SR208* and *SR209*) are small, two- to four-banded elements, not dissimilar to the *SR* derivatives of *TE146(Z)*. The others remain large insertions, with five to six bands, and retain the inverted repeat structure of their progenitor. However, they all appear to have internal rearrangements, perhaps small deletions. Finally, the two variegating derivatives of *SZ1*, *i.e.*, *SV200* and *SV201* are large, six- to eight-banded inverted repeats (Figure 5e).

DISCUSSION

The instability of *TE146*: G. ISING's family of transposable elements exhibits several different types of genetic instability (Fig. 6):

1. The *TE*s may be lost from the genome by excision. In the case of *TE146*, the frequency of spontaneous loss of w^+ is about one in 22,000 chromosomes. This frequency is about the same for both the tandem, *TE146(Z)*, and inverted, *TE146(Z)SZ1*, repeat forms of *TE146*, although the events are different genetically in the two cases. The *SW* derivatives of *TE146(Z)* have usually lost the entire element, those of *TE146(Z)SZ1* have not, since they retain cytologically visible bands. Loss may occur in either males or females. In males, loss is sometimes, perhaps always, premeiotic.

2. The *TE*s may transpose to new chromosome positions. It has been argued that at least some of the transpositions are duplicative (ISING and BLOCK 1981). The fact that *TE146-SR103* carries a new copy of w^+ shows that "half transposition" can occur from *TE*s that are duplicated for w^+. Both *TE146(Z)* and a new *TE* were recovered in *SR103*. This does not mean, however, that transposition was necessarily duplicative. Had this transposition occurred at the four-strand stage of mitosis, then a *TE* could have been excised from one chromatid and inserted into a sister chromatid that was subsequently recovered

through the germ line. In the example of *TE301*, however, the transposition could have occurred in a *TE146(Z)* homozygote and could, therefore, have occurred before chromosome replication. Evidence that transposition can follow excision comes from the studies of w^c, which, like *TE146*, is associated with *FB-NOF* sequences (PARO, GOLDBERG and GEHRING 1983). Transpositions of w^c were originally recovered with their reciprocal deletion of *w* (GREEN 1969). *Tp(1;3)*w^{zh} was also first recovered, on chromosome *3*, together with its reciprocal *Df(1)*w^{zh} (JUDD 1975). (However, the distal limits of *Df(1)*w^{zh} and *Dp(1;3)*w^{zh} are not identical at the molecular level, LEVIS, BINGHAM and RUBIN 1982). The loss of *TE146* from *noc* and the loss of those sequences that comprise *Tp* w^c*-1* and *Tp(1;3)*w^{zh} from *w* are equivalent events. Thus, the original transpositions of these elements, at least, followed excision, rather than being duplicative.

3. If transposition of a *TE* includes neighboring genetic material, then a genetically novel, and perhaps larger, transposing element may be formed (ISING and BLOCK 1981, 1984).

4. The *TE*s may undergo internal rearrangements. At least some of these may be scored easily by taking advantage of the interaction between the *TE*-borne *white* gene(s) on a *zeste* genetic background. Most *TE*s are one to two polytene chromosome bands. Some, for example *TE146(Z)*, are five to six bands and apparently arose by duplication or triplication of the smaller *TE*s. The duplicated forms of the *TE* may revert to the single form by "half loss." The frequency of "half loss" of *TE146(Z)* is high, about one in 1,700. The duplication of a single form is a relatively rare event, but can give rise to either tandem or inverted duplications. There is cytological evidence (Figure 5) that more complex forms of internal rearrangement of *TE146* can occur. However, only those that effect the expression of the genes carried by the *TE*, or at its insertion site, are readily detectable. Although the frequency of complete loss of w^+ is similar for the tandem (*TE146(Z)*) and inverted (*TE146-SZ1*) forms of this *TE*, the inverted form is far more stable with respect to loss of a single w^+ gene (*i.e.*, "half loss"). From *TE146(Z)* the frequency of spontaneous red derivatives is about one in 1,700, from *TE146-SZ1* it is about one in 10,000.

5. The *TE* may promote chromosome rearrangements. By selecting for the *SR* derivatives of *TE146(Z)*, two deletions (*SR48* and *SR54*) that begin within the *TE* and extend proximally into the adjacent chromosome region were recovered. Inversions that have one breakpoint within the *TE* and their second breakpoints elsewhere have also been recovered (associated with *SZ4* and *SR14*). It is curious that these two derivatives have similar, although not identical, breakpoints on chromosome arm *2R*.

Many, if not all, of the events that characterize the instability of *TE146* occur in the premeiotic germ line. The evidence for this statement is that clusters of identical exceptional progeny occur within the same cultures (Table 9). If so, then the types of event recoverable from *TE146* will be biased by germ line selection, as well as by zygotic aneuploidy.

***TE146* and *foldback* (*FB*) sequences:** PARO, GOLDBERG and GEHRING (1983) discovered that *TE*s of this family have *foldback* (*FB*) sequences (POTTER *et al.*

TABLE 9

A summary of the frequencies with which spontaneous derivatives of *TE146* occurred

Class of event	No. of chromosomes scored	No. of events	Clusters
TE146(Z)→TE146(Z)SW[a]	146,056	7	1 × 2, 1 × 3, 1 × 5
TE146(Z)→TE146(Z)SR	41,958	24	1 × 2, 1 × 3, 1 × 5
TE146(Z)SR23→TE146(Z:SR23)SW	6,894	1	
TE146(Z)SR36→TE146(Z:SR36)SW	7,921	0	
TE146(Z)SR100→TE146(Z:SR100)SW	18,110	0	
TE146(Z)SR23→TE146(Z:SR23)SZ	6,894	3	2 × 2
TE146(Z)SR36→TE146(Z:SR36)SZ	7,921	4	1 × 3
TE146(Z)SR100→TE146(Z:SR100)SZ	18,110	1	
TE146(Z:SR100)SZ1→TE146(Z:SR100:SZ1)SW	61,305	2	1 × 2
TE146(Z:SR100)SZ1→TE146(Z:SR100:SZ1)SR	61,305	6	2 × 2

[a] Data of GUBB *et al.* (1985), table 8, experiment 1.

1980) at their ends. Since *FB* sequences are transposable (POTTER *et al.* 1980; LEVIS, COLLINS and RUBIN 1982), it is reasonable to suppose that they cause the instability of the *TE* itself. *TE146* shows extensive homology to the FB8 clone by *in situ* hybridization (GUBB *et al.* 1985) and clearly carries both internal and terminal *FB* sequences. Exchange between the terminal elements would result in complete loss of the *TE*, and exchange between either terminal element and an internal element would result in "half loss." Complete losses (*i.e.*, the *SW* series, GUBB *et al.* 1985) would leave an *FB* element at the insertion site. In fact, all of the *SW*s derived from *TE146(Z)* retain between 3 and 10 kb of "foreign" DNA at the site of insertion of *TE146* within *noc*, and this DNA includes *FB* sequences (GUBB *et al.* 1985; CHIA *et al.* 1985b). Since all of the *SW*s derived from *TE146(Z)* are phenotypically wild type for *noc*, the noc phenotype associated with *TE146(Z)* must result from a position effect of the *TE* on *noc* or from an insertion of the *TE* into a noncoding region, rather than from a mutation of coding sequences.

Were "half loss" to result from exchange between an internal *FB* and a terminal *FB*, then two classes of *SR* derivative should be recovered, retaining the distal or proximal *white* genes. Cytologically there are two common types of *SR*, those with compact bands and those with more widely spaced bands (Figure 1). Whether these correspond to the two different "half losses" expected on the model is not certain. One surprising observation is that the frequency of "half loss" is ten times higher than the frequency of complete loss. There are several possible explanations of this observation. One is that the frequency of exchange between *FB* elements decreases with their distance apart (W. CHIA, personal communication); another is that the different *FB* elements of the *TE* differ in their structure and, hence, behavior. GOLDBERG *et al.* (1983) have also suggested that the frequency of asymmetrical exchange between repetitive elements may decrease with their distance apart. The fre-

quency of complete loss is too high to be accounted for by two independent "half loss" events.

However, there is one observation that makes it unlikely that "half loss" is, in fact, only due to exchange between *FB* sequences. Were it so, then the frequency of this event would not be expected to differ in *TE146(Z)* and *SZ1*, the tandem and inverted forms of *TE146*, respectively, because the *FB* element itself is an inverted repeat. Yet *SZ1* shows a very low frequency of "half loss." A possible explanation of the six-fold difference in "half-loss" frequency between *TE146(Z)* and *TE146-SZ1* is that "half losses" from *TE146(Z)* most frequently occur as the result of exchange between tandemly duplicated (but not *FB*) sequences that are inverted in *SZ1*. If so, the cytologically distinct classes of *SR* derivative of *TE146(Z)* may simply reflect different sites of exchange.

Male viable white-eyed derivatives of w^c are often deletions that extend between the *FB* element of w^c and another *FB* element 14 kb distal (COLLINS and RUBIN 1984). The generation of aberrations starting from *TE146(Z)*, however, cannot be explained by exchanges between a *TE*-associated *FB* element and a distant *FB* element. In the *TE146(Z)* chromosome there are about 18 different *FB* sites, as judged by *in situ* hybridization using FB8 as a probe (S. MCGILL and M. ASHBURNER, unpublished results). However, there is no *FB* sequence in this chromosome that could account for the proximal ends of the two deletions (*SR48* and *SR54*)—the nearest *FB* proximal to *TE146* is in 35EF, although an *FB* very close to the *TE* would be difficult to detect by *in situ* hybridization. It is unlikely that a second *FB* element is the cause of the *SR48* and *SR54* deletions, because the proximal limits of these two deletions differ with respect to unique DNA sequences (CHIA *et al.* 1985a); were they due to exchange with a nearby *FB*, they would be expected to be the same. The two inversions are both broken on chromosome arm *2R*, in region 42F-43B. There is an *FB* site within 43AB in the progenitor *TE146* chromosome, close, but clearly distal, to the inversion breakpoints. Moreover, the *2R* breakpoints of these two inversions differ, one being associated with a mutation of *pk*, the other not. It should be pointed out that there are *FB* elements between region 35 and 43B, for example in region 37, that have not been observed to recombine with those associated with the *TE*.

Single forms of *TE146*, *i.e.*, *TE146(Z)SR*, may duplicate spontaneously to form either tandem or inverted repeats. Tandem duplications might arise by unequal meiotic or mitotic exchange. However, such a mechanism cannot explain the inverted duplications, such as *TE146-SZ1*. Both types of duplication could result from transposition of the *TE* between homologous chromatids.

The *zeste-white* interaction: *TE146(Z)* carries two functional copies of *white* by five criteria: (1) It is cytologically a duplicated form of the *TE* and gives rise to smaller elements that retain a *white* allele (the *SR*s). (2) *w;TE146(Z)/+* flies have twice as much extractable eye pigment as *w;TE36(R)/+* flies (see GUBB *et al.* 1985). The *SR* derivatives fall into different classes with respect to the amounts of their eye pigments and whether or not they are dosage compensated for *white* (M. SHELTON, D. GUBB, J. ROOTE and M. ASHBURNER, unpublished results). The majority have approximately half as much pigment

as *TE146(Z)*. Those that do not cannot be suppressed by *zeste* and, presumably, retain two copies of w^+. Similar classes of *SR* were found as derivatives of both *TE146(Z)* and *TE146(Z:SR100)SZ1* (Tables 2 and 8). (3) z^1 w^{11E4}; *TE146(Z)/+* flies have zeste-colored eyes. (4) Two functional copies of *white* have been separated from *TE146(Z)* by gamma-ray-induced aberrations broken within the *TE* (D. GUBB, J. ROOTE, A. WILKINS and M. ASHBURNER, unpublished results). (5) *In situ* hybridization to *TE146(Z)* with a cloned probe for the *white* gene labels two distinctive sites within the *TE* (GUBB *et al.* 1985). Hybridization to *SR27* occurs only at one site (Figure 3b).

The suppression of w^+ by *zeste* requires the presence of two functional copies of w^+ (GANS 1953) or, at least, of the proximal part of *white* (GREEN 1959). Derivatives of white that cannot be suppressed by *zeste*, yet appear to be functional, by the criterion of pigment levels, have been recovered from both *TE36(R)* (*e.g.*, *TE36-RD1*, GUBB *et al.* 1984) and *TE146(Z)* (*e.g.*, *SR23*, *SR36*, etc.). It is interesting that *SR23* and similar derivatives are unstable with respect to their interaction with *zeste*, they give rise to forms that are *zeste*-suppressible at a high frequency (about one in 2,300, Table 9). This behavior is similar to that of the tandem duplication of *white*, $Dp(w^{sp})(w^{17G})$, studied by RASMUSON and his colleagues (RASMUSON, GREEN and KARLSSON 1974; RASMUSON and GREEN 1974). This duplication can exist in two interconvertible forms, red and zeste, according to the phenotype of males. The frequency of interconversion is high, about one in 3,000 for zeste → red and about one in 6,000 for red → zeste. As with *TE146*, this duplication can also suffer loss of one or other copy of *w* (RASMUSON and GREEN 1974; RASMUSON *et al.* 1981) and has given rise to a true transposon (RASMUSON *et al.* 1980). As with *TE146*, at least one member of RASMUSON's family of transposons also carried *FB* sequences (PARO, GOLDBERG and GEHRING 1983).

The nature of functional *white* alleles that cannot be suppressed by *zeste* is not known. In addition to those found as derivatives of *TE*, or RASMUSON's transposon (RASMUSON *et al.* 1980; HYLAND 1982), GREEN (1977) has recovered similar, although apparently stable, alleles of *white* as X-ray-induced derivatives of $Dp(1;1)w^{+R}$.

The genetic integrity of the proximal region of *white* is required for the interaction of *zeste* and *white* (GREEN 1959). RASMUSON and GREEN (1974) have suggested that the relative orientation of two copies of w^{prx} affects the sensitivity of the *w* genes of $Dp(w^{sp})(w^{17G})$ to the mutant *zeste* product. This is unlikely to be true for *TE146*, because (1) the *SR* derivatives that are red eyed when heterozygous with *TE146(Z)* carry two functional copies of *white*, and (2) the relative orientation of two *white* genes does not necessarily affect their interaction with *zeste* (*i.e.*, *TE146(Z)* and *TE146-SZ1*). It seems more probable, as suggested by RASMUSON *et al.* (1980, 1981), that the response of a *white* gene to *zeste* can be altered by the insertion, deletion or inversion of an element within w^{prx} without, necessarily, affecting other aspects of *white* function.

LEWIS (1954) coined the term "transvection" to describe the proximity dependent partial complementation of *Ubx* and bx^{34e}. Complementation between these alleles is weakened if the flies are also heterozygous for an aberration

with at least one breakpoint between the *BX-C* (in 89E) and the centromere of chromosome *3*. LEWIS interpreted this to mean that the complementation between these alleles depends on the synapsis of the homologues. Transvection is also known at the *decapentaplegic* locus (GELBART 1982; GELBART and WU 1982) and at *white* (GELBART 1971; JACK and JUDD 1979; BINGHAM 1981). At *white*, transvection is usually only obvious in the presence of z^1 (but see BINGHAM 1981), the suppression of *white* by *zeste* requiring two copies of w^+ that are physically close together. This physical proximity can be either *trans* or *cis*. The identical zeste phenotypes of z^1 w^{11E4}; *TE146(Z)/+* and z^1 w^{11E4}; *TE146(Z:SR100)SZ1/+* demonstrate that, when in *cis*, the two copies of *white* may be either tandemly repeated or inverted with respect to each other.

Heterozygotes between some adjacent *TE*s are phenotypically zeste on a z^1 w^{11E4} background (G. ISING, personal communication). This implies that these nonallelic *TE*s are close enough to pair. The effect can occur over at least seven polytene chromosome bands, since z^1 w^{11E4}; *TE36(R)/TE146(Z)* flies are *zeste*. Were transvection not occurring, then the single *white* gene of *TE36(R)* would not be suppressed, and these flies would have red eyes. Such is the case in *TE301*, *TE146(Z)/TE146(Z)* and *TE94(R)/TE146(Z)* heterozygotes, *TE94* and *TE146* are separated by 27 bands. However, this result must be interpreted with caution since *TE94* could be a member of that class whose w^+ gene(s) cannot be suppressed by *zeste*.

The *TE146-SR* derivatives were selected by their failure to be suppressed by *zeste*. With five exceptions they appear to be single copies of the *TE* that show transvection with both *TE36(R)* and with *TE146(Z)*, but not with *Dp(1;1)*w^{+R}. The five exceptional chromosomes (*SR23*, *SR36*, *SR45*, *SR103* and *SR104*) remain red eyed when heterozygous with *TE36(R)*, *TE146(Z)* and *Dp(1;1)*w^{+R}. This results from a dominant suppressor of *zeste* on the *TE* chromosome. One type of dominant suppressor would result from the transposition of half of *TE146(Z)*, carrying one copy of w^+, to another site on the second chromosome (as in the case of *SR103*). These "half-jump" *TE*s would carry one copy of w^+ and would be expected to give a zeste phenotype when homozygous. In four cases, however, it was not possible to separate the dominant supressors of *zeste* from *TE146* by recombination. This suggests that one of the *TE*s *white* genes is no longer affected by transvection and fails to be suppressed by *zeste*, even when "paired" with an active w^+ gene. It is consistent with this interpretation that the exceptional *SR*s that cannot be suppressed by *zeste* express the same amount of pigment as the parental *TE146(Z)*, whereas other *SR*s express approximately half as much pigment. There is one exception to this rule, *SR14*, which has the same amount of pigment as *TE146(Z)*, but is not suppressed by *zeste*. *SR14* is the only *SR* chromosome that carries an associated inversion, a breakpoint of which is within the *TE*. This breakpoint carries rst^+, but not w^+, to chromosome arm *2R*. Therefore, assuming that the high pigment level of *SR14* is the result of two functional copies of w^+, these genes must remain outside the inversion. However, both copies of w^+ are capable of being suppressed by *zeste* when heterozygous with *TE146(Z)* or *TE36(R)*. This implies that the *cis* and *trans* interactions between *white* genes may not be equivalent,

since the former, but not the latter, is affected by the *SR14* inversion breakpoint.

***TE146* and the *noc* locus:** *TE146(Z)* is inserted into the *noc* locus by the criteria that *noc* and *TE146* map to cytologically coincident positions and that *TE146* is associated with a mutation of *noc* that reverts when the *TE* is lost (GUBB *et al.* 1985). Not surprisingly, the spontaneous red (*SR*) derivatives of *TE146(Z)* remain strong *noc* alleles and retain the other genetic properties associated with such alleles, *i.e.*, lethality with $l(2)br29^{ScoR+1}$ and strong dominant enhancement of *Sco* (Table 3). The behavior of the spontaneous white and spontaneous red derivatives of *TE146-SZ1* was, however, quite unexpected. Four of the five spontaneous white derivatives of *SZ1* remain strong *noc* alleles, strong enhancers of *Sco* and are lethal with $l(2)br29^{ScoR+1}$ (Table 7). This is quite different from the behavior of spontaneous white derivatives of *TE146(Z)*, all of which are noc^+ and no longer interact with *Sco* or $l(2)br29^{ScoR+1}$ (GUBB *et al.* 1985). The *SW* derivatives of *SZ1* may also differ from those of *TE146(Z)* in retaining cytologically evident bands at 35B1.2. Clearly the spontaneous white-eyed derivatives of *TE146(Z)* and *TE146(Z:SR100)SZ1* are quite different.

The properties of some of the spontaneous red derivatives of *SZ1* were also unexpected. Of the seven studied, five are similar to *TE146(Z)SR*s, in showing the genetic properties associated with the strong *noc* allele of *TE146(Z)*. Two (*SR204* and *SR205*) differ—both retain a cytologically evident insertion at 35B1.2, but are only weak alleles of *noc* and weak dominant enhancers of *Sco*. Furthermore, both are viable with $l(2)br29^{ScoR+1}$ (Table 7).

These data strengthen our previous conclusion (GUBB *et al.* 1985; CHIA *et al.* 1985b) that the mutation of *noc* associated with the insertion of the *TE* cannot be due to a change within the *noc* gene's coding region, but must be a position effect of the *TE* or an insertion into noncoding sequences. However, the precise details of the mechanism of this mutation must await thorough molecular analysis of the *noc* gene.

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