THE GENETICS OF A SMALL AUTOSOMAL REGION OF *DROSOPHILA MELANOGASTER* CONTAINING THE STRUCTURAL GENE FOR ALCOHOL DEHYDROGENASE. III. HYPOMORPHIC AND HYPERMORPHIC MUTATIONS AFFECTING THE EXPRESSION OF HAIRLESS

MICHAEL ASHBURNER

Department of Genetics, University of Cambridge, Cambridge, England

Manuscript received December 10, 1981
Revised copy accepted April 14, 1982

ABSTRACT

A lethal locus (*l(2)br7*;35B6-10), near *Adh* on chromosome arm *2L* of *D. melanogaster*, is identified with Plunkett's dominant suppressor of Hairless (*H*). Of eight new alleles, seven act as dominant suppressors of *H*, the eighth is a dominant enhancer of *H*. One of the suppressor alleles is both a leaky lethal and a weak suppressor of *H*. Confirming NASH (1970), deletions of *l(2)br7* are dominant suppressors, and duplications are dominant enhancers of *H*. A simple model is proposed to account for the interaction of *l(2)br7* and *H*, assuming that amorphic (or hypomorphic) alleles of *l(2)br7* suppress *H* and that hypermorphic alleles enhance *H*.

LOCUS and allele specific suppressor and enhancer mutations are well known in *Drosophila melanogaster*, although there is little evidence for any particular example of the molecular basis of the specific interaction between suppressor (or enhancer) and suppressed (or enhanced) alleles (see KAUFMAN, TASAKA and SUZUKI (1973) for review). NASH (1970) described the dominant suppression of the phenotype of Hairless by a deficiency of chromosome arm *2L* that included a previously identified dominant suppressor of Hairless (*Su(H)*). In the same paper NASH also gave evidence that duplications for the same chromosome region act as dominant enhancers of the Hairless phenotype. In this paper I present a further analysis of the suppression and enhancement of Hairless by *Su(H)* and its alleles and show that a lethal allele of *Su(H)* can act as a dominant enhancer of Hairless.

MATERIALS AND METHODS

Four alleles of the third chromosome dominant mutation Hairless were used in this study. Both H^1 and H^2 are old alleles and were included by PLUNKETT (1926) in his classic study of Hairless. Both are of spontaneous origin. The H^1 allele was on a third chromosome marked with both *Gl* and *Sb* or *Gl* alone. H^{57} is associated with $Tp(3)H^{57}$ (VAN BREUGEL, RAY and GLOOR 1968), which has the new gene order: 61-86F7-11/97D1.2-95C1.2/98C5-97D1.2/86F7.11-95C1.2/98C5-100. Since *H* is not included within the deficiency segregant of *T(1;3)05* (*i.e.*, *Df (3R)88C;92CD*) and since *H* maps proximal to ebony (BRIDGES and MORGAN 1923), which is

in 93D2.3 (HENIKOFF 1980), I can only presume that $Tp(3)H^{57}$ and H^{57} are independent mutational events. A deletion of 92CD to 93F;94A is phenotypically Hairless (LINDSLEY *et al.* 1972) while *e* deletions extending proximal to 93A5-B1 (*i.e.*, *Df(3R)e100.256*) are not said to be *H*. *H* is, then, presumably between 92CD and 93B. H^{80} was discovered by chance during this study (by G. HARRINGTON) and was induced by treatment of males with 4500 R of gamma rays. It is cytologically normal. All *H* alleles are recessive lethal and lethal *inter se*. Other stocks are listed in Table 1.

The phenotype of *H* flies was scored by counting the occupancy of the 40 major dorsal head and dorsal thoracic macrochaetae, *i.e.*, the anterior, middle and posterior orbitals (AO, MO, PO), the anterior and posterior verticals (AV, PV), the ocellars (O), the postverticals (PVt), the presuturals (PSt), the upper and lower humerals (UH, LH), the anterior and posterior notopleurals (AN, PN), the anterior and posterior postalars (AP, PP), the anterior and posterior supraalars (AS, PS), the anterior and posterior dorsocentrals (AD, PD) and the anterior and posterior scutellars (ASc, PSc).

RESULTS

Phenotypes of Hairless

PLUNKETT (1926) described the pattern of bristle loss in flies heterozygous for either H^1 or H^2. Both genotypes are characterized by the absence of specific major bristles, although the bristle sockets usually remain. It is striking that the pattern of bristle loss in H^1 remains very similar to that described by PLUNKETT more than 50 years ago (Table 2). $H^1/+$ heterozygotes usually lack 10 to 15 bristles: the PO, PVt, UH, PP and AD are the preferred sites of loss. The phenotypes of the three other *H* alleles are very similar; all show a loss of 7 to 12 bristles per fly and the pattern of loss in all three alleles resembles that of H^1. Table 2 also shows the pattern of bristle loss in suppressed and enhanced H^1.

In addition to their effects on macrochaetae, all *H* alleles are recessive lethal, remove microchaetae (for example, the acrostichial rows) and have an effect on wing veination, most obvious as a shortening of the *L5*.

Neither *Su(H)* nor any of its lethal alleles show any phenotype other than recessive lethality in the absence of *H* (but see below with regard to the *LT3* and *BMW4* alleles). Besides affecting the expression of *H*, all alleles of *Su(H)* tend to enhance the wing-vein phenotype of *H* alleles.

Table 2 shows that *Su(H)*/+;*H*/+ heterozygotes have seven to ten more bristles than their *Cy*/+;*H*/+ siblings (see also Table 3). On the other hand, enhanced *H* genotypes have 10 to 15 fewer bristles than their *Cy*/+;*H*/+ siblings, and a far more extreme loss of microchaetae on the thorax.

The l(2)br7 *locus*: GRELL (in LINDSLEY and GRELL 1968) mapped the dominant suppressor of Hairless, *Su(H)*, to *Df(2L)64j*, a 34-band deletion on chromosome *2L*. Subsequently, NASH (1970) found that this deficiency itself acted as a dominant suppressor of *H*. I have confirmed both observations and identified eight more alleles of *Su(H)* among a set of some 200 lethals mapping to the *Df(2L)64j* region. In addition, O'DONNELL *et al.* (1977) found three more alleles of *Su(H)*. Of the alleles I have studied, six were induced with ethyl methanesulphonate, one *(SF8)* was triethylenemelamine-induced and one *(AR9)* was found in a chromosome extracted from a natural population from Greece. The nine available alleles all fall into a single lethal complementation group and seven of them are completely lethal *inter se*. The exceptions are *LT3* which has,

TABLE 1

Genotypes of stocks used

(a) *l(2)br7* alleles

l(2)br7$^{Su(H)}$ l(2)br36$^{Su(H)}$ l(2)Su(H) whd^{1}/CyO
l(2)br7^{AR9}/CyO
Adh^{uf3} l(2) br7^{SF8} cn/CyO
Adh^{n11} l(2)br7^{LT3} l(2)CA5^{LT3} cn vg/CyO
Adh^{n1} l(2)br7^{HG3} rd^{s} pr cn/CyO
Adh^{n10} l(2)br7^{HG36} cn vg/CyO
b l(2)br7^{S6} pr/CyO
Adh^{uf3} l(2)br7^{BMW9} rd^{s} pr cn/CyO
Adh^{uf3} l(2)br7^{BMW4} rd^{s} pr cn/CyO

(b) Control chromosomes

b pr
Adh^{D} l(2)br26^{OK5} pr cn/CyO, Adh^{nB}
Adh^{D} l(2)br27^{CH52} pr cn/CyO, Adh^{nB}
b Adh^{n4} l(2)br^{SF1B}/CyO

(c) Deletions

Df(2L)64j L^{2}/CyO = Df(2L)34D1.2; 35B8.9–C1
Df(2L)75c/CyBl = Df(2L)35A1.2; 35D4.7 + In(2L)27D1.2; 35A1.2
Df(2L)AR–R1, y+ac+/CyO = Df(2L)35A3.4; 35B8.9–C1
b Df(2L)A376 cn bw/CyO, Adh^{nB} = Df(2L)34E3; 35C4.5
Df(2L)TE36–GA pr pk cn/CyO (not cytologically deficient)
Df(2L)TE36–GC pr pk cn/CyO = Df(2L)35C1; 35D2
Df(2L)TE36–GD pr pk cn/CyO = Df(2L)35B4; 35C3
Df(2L)fn3 pr cn/CyO, Adh^{nB} = Df(2L)35B1; 35B3.4
Df(2L)fn7 pr cn/CyO, Adh^{nB} = Df(2L)34E1.2–4.5; 35B3–4.5
Df(2L)fn27 pr cn/CyO, Adh^{nB} = Df(2L)35B1; 35D1.2
Df(2L)fn31 pr cn/CyO, Adh^{nB} = Df(2L)34D3; 35B3–5
Df(2L)el^{77} Coi/Gla = Df(2L)35A1; 35B2
C(1)RM,y; T(Y;2) J165^{P},B^{S}; T(Y;2)P58^{D}, y+/CyO = Df(2L)35C4.5; 35D5–7
Df(2L)C158.1^{L}Sco^{R+17R}, pr/CyO = Df(2L)35B3; 35C + Dp(2;2)25D3–7; 26D1.2 + In(2L)25D3–7; 35B3
Df(2L)Sco^{R+23} pr/CyO = Df(2L)34F1.2; 35C1.2

(d) Duplications

Dp(2;2)C163.41^{L} C158.1^{R}/CyBl = Dp(2;2)35B3; 35E1.2 + Dp(2;2)26D1.2; 27D1.2 + In(2L)26D1.2; 35E1.2
Dp(2;2)Sco^{R+17L} C158.1^{R}, b/Gla = Dp(2;2)35B3; 35C + Df(2L)25D3–7; 26D1.2 + In(2L)26D1.2; 35C
Dp(2;1)Sco^{R+23}; el+ rd+; b el rd^{s} pr cn = Dp(2;1)34F1.2; 35C1.2; 20
Dp(2;2)Adh^{s}, (b+ rk^{EMS} el+ Adh^{D})(b rk+el Adh^{F}), rd^{s}L^{2}(l)/CyO = Dp(2;3)34B1.2; 35B3
Dp(2;2)GYL, b+rd+, dp b cn bw/CyRoi = Dp(2;2)33B1.2; 35C1.3; 50A4–B5
Dp(2;2)GYS, b+rd+, dp b cn bw/CyO = Dp(2;2)34D1.2; 35C1.3; 50A4–B5

(e) Hairless stocks

G1 Sb H^{1}/In(3L + 3R)P (l)
G1 H^{1}/In(3LR)TM3, Sb Ser
H^{2}/T(2;3)ap^{Xa}
H^{80}/In(3LR)TM3, Sb Ser
Tp(3)H^{57}/Ubx

Note *CyO = In(2LR)O, Cy dp^{lvl} pr cn^{2};*
CyBl = In(2L)Cy + In(2R)Cy, al^{2} Cy pr Bl cn^{2} c vg sp^{2};
CyRoi = In(2L)Cy^{L}l^{R}, Cy b$^{77.1x}$ Roi + In(2R)Cy, bw sp^{2} or;
Gla = In(2LR)Gla, Gla l(2)br16^{SF16} l(2)br3^{TA2}

TABLE 2

Pattern of loss of macrochaetae from the dorsal head and thorax in Hairless genotypes

Macrochaetae	Genotype*							
	H^1	H^1	H^2	H^{87}	H^{80}	$Su(H);H^1$	$S5;H^1$	$LT3/SF8$
AO	0.85	0.95	0.95	0.95	0.88	1.00	*0.32*	*0.00*
MO	1.00	0.83	1.00	0.98	1.00	0.91	*0.58*	*0.00*
PO	*0.25*	*0.60*	*0.70*	*0.44*	*0.34*	0.94	*0.00*	*0.00*
O	0.99	1.00	1.00	0.83	0.96	0.98	*0.40*	*0.00*
AV	*0.43*	0.88	0.96	0.86	*0.70*	1.00	*0.00*	0.94
PV	0.85	*0.33*	*0.73*	*0.71*	*0.28*	1.00	*0.00*	*0.61*
PVt	*0.00*	*0.03*	*0.03*	*0.01*	*0.00*	0.96	*0.00*	*0.00*
PSt	*0.68*	0.85	0.95	*0.60*	*0.60*	1.00	*0.03*	*0.78*
UH	*0.25*	*0.45*	*0.78*	*0.46*	*0.28*	0.99	*0.00*	*0.00*
LH	0.93	1.00	1.00	1.00	0.99	1.00	*0.73*	*0.00*
AN	1.00	1.00	1.00	1.00	1.00	0.99	0.95	*0.06*
PN	1.00	1.00	1.00	1.00	1.00	1.00	0.95	*0.00*
AS	1.00	1.00	1.00	1.00	1.00	1.00	*0.63*	*0.00*
PS	0.95	*0.60*	*0.38*	0.99	*0.05*	0.86	*0.58*	*0.00*
AP	1.00	0.98	1.00	1.00	1.00	1.00	*0.03*	*0.00*
PP	*0.55*	*0.43*	*0.69*	0.91	*0.38*	*0.64*	*0.60*	*0.00*
AD	*0.60*	*0.80*	0.84	0.84	*0.66*	0.86	*0.00*	*0.00*
PD	1.00	1.00	1.00	1.00	1.00	0.96	*0.48*	*0.00*
ASc	0.99	*0.60*	0.95	1.00	0.94	*0.79*	0.88	*0.00*
PSc	1.00	0.88	1.00	1.00	1.00	0.94	0.98	*0.39*
mean	30.64	30.30	33.38	33.58	27.98	37.60	16.30	5.56
s.e.	—	0.59	0.27	0.31	0.28	0.19	0.68	0.34
N	—	20	40	40	40	40	20	9

The first H^1 column is data calculated from Plunkett (1926) Table 1 column 9. The second H^1 column is the present data from a *Gl Sb* H^1 stock. Bristle sites with less than 80% occupancy are in italics. The final column illustrates the fact that $l(2)br7^{LT3}$ escapers (in this case $l(2)br7^{LT3}/l(2)br7^{SF8}$) have a different pattern of bristle loss from enhanced *H* phenotypes (compare, for example the AV, PV and PSt sites, all with a higher occupancy in *LT3/SF8* escapers than in *S5*; H^1 despite the far lower mean bristle number in the former genotype).

on rare occasions, given viable escapers with some other *Su(H)* alleles; and *BMW4*, a leaky lethal. The *LT3* escapers (6/586 with *Su(H)*, 11/614 with *SF8*, lethal with *AR9*, *BMW9*, *HG36*, *HG3* and *S5*), have an extreme mutant phenotype: their wings and halteres are similar to those of an extreme vestigial allele; their eyes, although large, have a rough glazed appearance and the flies are almost acheatous, having fewer than ten macrochaetae per fly. The acrostichial hairs, and other microchaetae (*e.g.*, frontals, interocellars), are reduced in number and disturbed in arrangement. The tarsal claws are also much reduced in *LT3* escapers. Similar flies have been seen when *LT3* is heterozygous with $Su(H)^-$ deletions (Table 5). The resemblance between the bristle phenotype of *LT3* escapers and Hairless is superficial; the pattern of bristle loss is quite different in these genotypes (Table 2). The *BMW4* allele is clearly leaky. When heterozygous with *Su(H)* it survives at 20% of its expected frequency (47/653); similarly *BMW4* is semilethal with *AR9*, *SF8*, *BMW9* and *HG36*, almost viable with *LT3* (209/814) and lethal with *S5* (0/521). Heterozygotes

TABLE 3

Effects of l(2)br7 *alleles and control chromosomes on the expression of H*†*

	Cy+			Cy			
	N	$\bar{x}$	*s.e.*	N	$\bar{x}$	*s.e.*	Difference
(a) *l(2)br7* alleles							
Su(H)	40	31.85	0.52	40	25.05	0.38	+ 6.80
AR9	40	37.33	0.21	40	26.85	0.41	+10.48
SF8	40	35.43	0.24	40	27.05	0.42	+ 8.38
LT3	20	36.70	0.47	20	27.30	0.61	+ 9.40
HG3	20	36.40	0.40	10	26.70	0.98	+ 9.70
HG36	20	39.24	0.18	20	32.20	0.39	+ 7.04
BMW9	20	35.85	0.41	10	26.20	0.92	+ 9.65
BMW4	20	30.60	0.51	20	26.20	0.53	+ 4.40
S5	40	14.00	0.33	40	26.48	0.45	−12.48
(b) Control chromosomes							
$l(2)br2^{SF18}$	40	24.28	0.36	20	23.85	0.47	+ 0.43
$l(2)br26^{OK5}$	10	27.00	0.67	10	28.00	0.99	− 1.00
$l(2)br27^{CH52}$	10	28.60	0.82	10	28.50	1.16	+ 0.10
b pr	40	22.58	0.42	20	23.38	0.45	− 0.80

* Both *Cy/+;Gl Sb H/+* and *Cy+/+;Gl Sb H/+* siblings from a cross of *l/Cy*; +/+ × +/+; *Gl Sb H/In(3L + 3R)P* were scored for bristle number.

† The viability of all *l(2)br7/+;Gl Sb H/+* genotypes was normal with the exception of *HG36* whose relative viability with *Gl Sb H* was only 4% rather than the expected 25% (N = 632). However this allele was not semilethal with H^2, H^{57} or H^{80}, and the reason for its interaction with respect to viability with *Gl Sb H* has not been studied.

between *BMW4* and other *Su(H)* alleles have vestigial wings (and halteres), eyes that are somewhat reduced and rough, but normal bristles. Thus the *BMW4* escaper phenotype is far less extreme than that of *LT3*. The wing phenotype of these escapers is not due to a mutant *vg* locus.

In a small experiment to recover new lethal alleles of *Su(H)* after EMS treatment of *b pr* males, one lethal chromosome (in 403) was recovered. Unlike all other lethal alleles of *Su(H)*, this chromosome *(S5)* acts as a dominant enhancer of Hairless.

As indicated in Table 3, all lethal alleles of *Su(H)*, with the notable exception of *S5*, act as dominant suppressors of *H* and do so to a degree quantitatively similar to that of *Su(H)* itself, adding between seven and ten bristles per fly to the *H* phenotype. The effects of the new lethal alleles of *Su(H)*—including *S5* —on H^2, H^{57} and H^{80} are similar to their effects on H^1 (Table 4). The suppression of *H* by the leaky allele *BMW4* is less than that by the other alleles (Table 4; a repeat cross gave a suppression of H^1 by +4.0 bristles.

The lethal periods of three lethal *Su(H)* alleles have been determined as hemizygotes. Two suppressor alleles (*Su(H)* and *SF8*) and the enhancer *S5* are all pupal lethals. Larval development and pupariation is not delayed and normal puparia form; yet hemizygotes for all three alleles die in the period between

TABLE 4

Effects of l(2)br7 *mutations on the expression of H alleles**

l(2)br7	Allele			
	H^1	H^2	H^{57}	H^{80}
Su(H)	+ 6.80	+ 5.69	+ 7.40	+ 9.80
HG36	+ 7.04	+ 6.10	+ 8.20	+ 9.80
Df(2L)64j	+ 8.60	+ 5.95	+ 8.25	+ 8.85
S5	−12.48	−12.20	−12.80	− 9.90
Dp(2;2)C164.41^{L}C158.1^{R}	−12.90	−13.38	−12.05	−10.80

* Shown as the difference in bristle number between *mutation/+;H/+* and *Cy/+;H/+* siblings . At least 20 flies counted per cross.

head eversion and the beginning of eye pigmentation. *LT3* and *BMW4/Df* flies often die as pharate adults or very soon after eclosion.

Since not all lethal alleles of *Su(H)* are suppressors of *H*, we refer to this locus as *l(2)br7* (WOODRUFF and ASHBURNER 1979b).

Mapping of l(2)br7: Following GRELL's discovery (in LINDSLEY and GRELL 1968) that *Su(H)/Df(2L)64j* heterozygotes are lethal WOODRUFF and ASHBURNER (1979b) crossed several deficiencies that overlapped *Df(2L)64j* with *Su(H)* and its lethal alleles then available and showed that the cytological position of *Su(H)* was between bands 35B3 and 35B10 (see also NASH 1970). Since then many new deletions in region 35 have become available, in particular, several that overlap the right hand part of *Df(2L)64j*; these allow better genetic and cytological mapping of *l(2)br7* to 35B6-9. The present map of this small region is shown in Figure 1. No deficiency end points that separate *l(2)br7* from *l(2)br26* have been recovered, but these two loci complement fully for viability and *l(2)br26* alleles have no effect on the expression of *H* (Table 3).

I mapped *SF8* by recombination with *l(2)br4^{AR1}*, a lethal complementation group that maps 0.46 map units proximal to *Adh* (2:50.1). The *AR1–SF8* distance was 0.25 map units (n = 7189) putting *l(2)br7* at approximately 50.8 (using the *Adh* position as reference).

Heterozygotes between *l(2)br7* alleles and *l(2)br7^{-}* deletions are invariably quite lethal—except for *LT3* which rarely escapes, and then only over *Df(2L) TE36-GA*, and *BMW4* which occasionally escapes (28/4355), over various deletions. The phenotypes of *LT3/Df* and *BMW4/Df* escapers resembles those, described above, of *LT3/l(2)br7* and *BMW4/l(2)br7* respectively.

Deficiencies and H *expression*

Nearly 70 different deficiencies for various parts of section 35 of chromosome arm *2L* have been tested for their effects on the expression of *H*. Without exception, those that include *l(2)br7* act as dominant suppressors of *H*, and those that are *l(2)br7^{+}* do not. Some representative data is shown in Table 5.

Duplications and H *expression*

NASH's (1970) enhancer of Hairless was characterized cytologically as a small duplication, for bands 35B6 to 35B10. NASH (1970) also found that two other

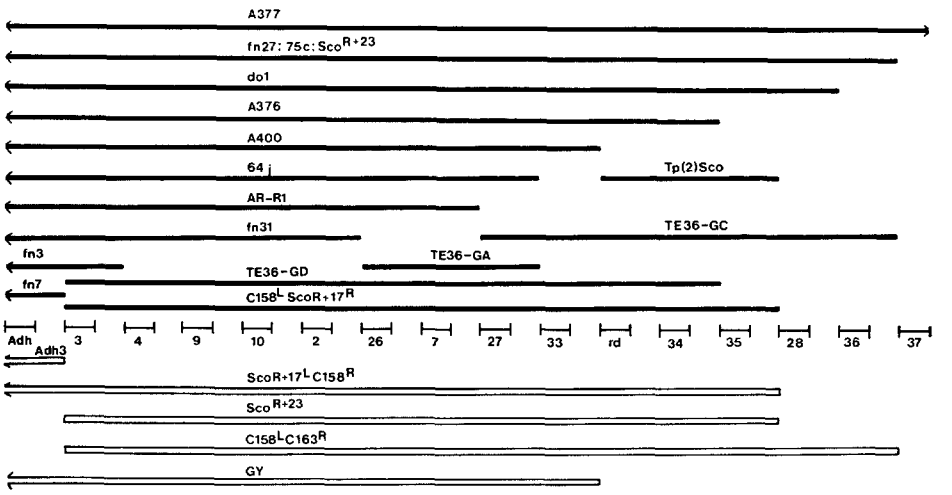

FIGURE 1.—Genetic map of the *l(2)br7* region. With the exception of reduced (*rd*) and *Adh* all of the loci are known from recessive lethal alleles. The deletions are described in Table 1 except *Df(2)A377* (= *Df(2L)34F1.4*; *35F1.4*), *Df(2L)A400* (= *Df(2L)35A1.4*; *35B10*) and *Df(2L)Sco*, a deletion synthesized as a crossover between *Tp(2)Sco* (= *Sco*) and a wild-type homolog by G. MARONI (unpublished). The proximal limits of *Dp(2;1)Sco*$^{R+23}$ and its corresponding deficiency (*Df(2L)Sco*$^{R+23}$) differ. The *TE36-G* deletions were induced (with gamma rays) by selecting the loss of a w^{+} rst^{+} transposing element inserted in *l(2)br27*. *Df(2L)AR-R1* was synthesized from the deletion *T(Y;2)A80*^{P}; *T(Y;2)R15*^{P} (WOODRUFF and ASHBURNER 1979a). The *Df(2L)fn*'s were formaldehyde-induced (O'DONNELL *et al.* 1977) and the *Df(2L)A*'s X-ray-induced (AARON 1979), both series selected as ADH negatives. The region between *Adh* and *l(2)br37* is approximately 35B2.3 to E1.2. The *l(2)br*'s are indicated only by their numbers. Solid bars are deletions, open bars duplications. *Df(2L)el*^{77} shares its proximal breakpoint with *Df(2L)fn7*.

duplications acted as dominant enhancers of Hairless; they were *Dp(2;2)Adh2* and *T(2;3)DpAdh1* described as *Dp(2;2)32D3;35C1* and *Dp(2;2)35A;35D* respectively. Unfortunately, *E(H)* and *Dp(2;2)Adh2* are lost, and our stock of *T(2;3)DpAdh1*, although *T(2;3)33E9;89A3.7* is not duplicated on *2L*, nor is it an enhancer of *H*.

However, four new duplications for region 35 have been made or identified. *Dp(2;2)C163.41*^{L}*C158.1*^{R} and *Dp(2;2)Sco*$^{R+17L}$*C158.1*^{R} are exchange products between *In(2L)C158.1* (= *In(2L)26D1.2;35B3*) and *In(2L)C163.41* (=*In(2L)27D1.2;34E1.2)* or *In(2L)Sco*$^{R+17}$ (= *In(2L)25D3.7;35C*) respectively. *Dp(2;1)Sco*$^{R+23}$ is a segregant from *T(2;1)Sco*$^{R+23}$, an X-ray-induced revertant of Scutoid that is, cytologically, *Df(2L)34F1.2;35C1.2;T(2;1) 34F1.2;35C1.2;20*. The *X*-linked duplication appears, in polytene nuclei, as a small banded chromosome fragment usually associated with the nucleolus. The duplicated segregant is both male and homozygous-female viable and fertile. *Dp(2;2)GY* was found by YANNOPOULOS *et al.* (1981) as an apparent male double crossover between a *dp b cn bw* chromosome and the *Mr* element *Mr.23.5*. In fact it was not a regular crossover, but it did contain a duplication of b^{+} (from the *Mr.23.5* chromosome) inserted into the marker chromosome at 50A4-B5 (YANNOPOULOS *et al.* 1981). Subsequent to its isolation, the duplication underwent a deletion

TABLE 5

Effect of deficiencies for region 35 on the expression of H *and viability of* l(2)br7 *heterozygotes**

Heterozygote	*Df/+; H/+* N	$\bar{x}$	*s.e.*	*Cy/+; H/+* N	$\bar{x}$	*s.e.*	Difference	*Df/l(2)br7*
Df(2L)64j	20	37.80	±0.50	20	29.20	±0.90	+ 8.60	0/3620
Df(2L)75c	40	36.25	±0.33	20	23.55	±0.44	+12.70	0/2619
Df(2L)AR-R1	25	37.32	±0.35	25	25.88	±0.38	+11.44	0/2452
Df(2L)A376	20	35.85	±0.64	20	29.90	±0.53	+ 5.95	0/334
Df(2L)fn27	20	34.95	±0.28	20	29.90	±0.51	+ 5.05	0/414
Df(2L)C158.1^{L}ScoR+17^{R}	33	35.88	±0.30	40	31.71	±0.43	+ 4.17	0/211
Df(2L)TE36-GA	20	34.70	±0.44	10	28.20	±0.93	+ 6.50	53/3050†
Df(2L)TE36-GD	20	34.05	±0.54	20	24.45	±0.64	+ 9.60	0/585
Df(2L)fn3	25	28.04	±0.45	25	28.32	±0.49	− 0.28	893/2831
Df(2L)fn7	25	27.04	±0.35	25	28.84	±0.43	− 1.80	317/1142
Df(2L)el77	40	29.98	±0.31	40	29.38	±0.29	+ 0.60	333/1210
Df(2L)fn31	40	25.73	±0.35	40	27.30	±0.37	− 1.57	860/3130
Df(2L)J165^{D}P158^{P}	20	25.55	±0.53	10	24.90	±0.52	+ 0.65	—
Df(2L)TE36-GC	20	24.29	±0.61	20	24.58	±0.52	− 0.29	291/921‡

* See Table 1 for deficiency break points. Bristle data is a comparison of the *Cy/+; Gl Sb H/+* and *Df/+; Gl Sb H/+* siblings from crosses of *Cy/Df* × *Gl Sb H/In(3L+3R)P*. Viability data is summed over several *l(2)br7* alleles and is from crosses of *Df/Cy* × *l(2)br7/Cy*. It is expressed as the number of *Df/l(2)br7* flies over total progeny number. Data from *BMW4* crosses not included.

† All escapers from crosses with *LT3*, see text.

‡ *Su(H)/Df(2L) TE36-GC* are lethal due to *l(2)br36$^{Su(H)}$*, a second lethal on the *Su(H)* chromosome included in *Df(2L)TE36-GC*; data from this cross are not included.

and is now in two forms, one (*Dp(2;2)GYL*) is 21-50A4/35C1.3-33B1.2/50B1.5-60 and the other (*Dp(2;2)GYS*) is 21-50A4/35C1.3-34D1.2/50B1.5-60. With respect to their interaction with *H*, the long and short forms of *Dp(2;2)GY* behave similarly.

Since the region 35 breakpoints of component inversions of the two *In(2L)C158.1* crossovers (*i.e.*, *In(2L)C158.1* itself, *In(2L)C163.41* and *In(2L)Sco^{R+17}*) have also been used to construct synthetic deficiencies the precise genetic limits of these two duplications are known (Figure 1). Similarly, the genetic limits of *Dp(2;1)Sco^{R+23}* were determined by finding which lethals and deficiencies this *X*-linked duplication can cover (Figure 1). The proximal limit of the *Dp(2;2)GY*'s lie between *l(2)br33* and *l(2)br34* determined by crossing *Df(2L)75c Dp(2;2)GY/CyO* to representative lethal alleles of loci included within *Df(2L)75c*.

All four duplications act as strong enhancers of H^1 and, with respect to *Dp(2;2)C163.41^{L}C158.1^{R}* (at least), of the other three *H* alleles (Table 6). For *Dp(2:2)Sco^{R+17L}C158.1^{R}* its reciprocal exchange product, *i.e.*, *Df(2L)C158.1^{L}-Sco^{R+17R}*, is a suppressor of *H*. *Df(2L)Sco^{R+23}* is also a dominant suppressor of *H*. Flies that carry both the *Sco^{R+23}* duplication and the corresponding deletion have a normal *H* phenotype.

Since *Dp(2;1)Sco^{R+23}* females are homozygous viable and fertile we can study the effects of two doses of the duplication on *H* expression. As shown in

Table 6 *Dp/Dp;+/+;H/+* flies have a very extreme *H* phenotype, with only 9 to 10 bristles per fly. A similar phenotype is seen in flies carrying one dose of the duplication on their *X* chromosome and the enhancer of *H* allele *l(2)br7*^{S5} on chromosome *2* (Table 6). A graph of the number of doses of *Su(H)*$^{+}$ and their effect on *H* expression is linear (Figure 2). The enhancing allele of *l(2)br7* (*S5*) acts quantitatively, as if it were a duplication for *Su(H)*$^{+}$ and the suppressing alleles (except *BMW4*) as if they were *Su(H)* deletions (see below).

All of the four duplications have a very slight effect on bristle number in the absence of an *H* allele; for example, *Dp(2;2)GYL/Dp(2;2)GYS* flies have a mean of 39.96 ± 0.02 ($n = 80$) bristles per fly. It is difficult to know whether or not this very slight reduction in bristle number is biologically "significant." Two facts suggest that it may be: in wild-type flies the number of dorsal head and thoracic macrochaetae is remarkably constant, and in all the duplications studied here it is the PVt bristle that is lost, one of the most "sensitive" sites for loss in *H* genotypes.

As a control I used (Table 6) GRELL's (NASH, 1970) *Dp(2;2)Adh3*, a duplication whose genetic limits have not been determined but which, cytologically, does not extend proximal to 35B3. It is not an enhancer of *H*; in fact, as NASH (1970) also found, it acts as a slightly dominant suppressor of *H*.

A final comment is needed regarding the enhancer of *H* allele, *l(2)br7*^{S5}. Since *S5* has an effect on *H* similar to duplications for *Su(H)*$^{+}$, it might be argued that it is itself an EMS-induced duplication. The polytene chromosomes of *S5* appear to be quite normal and *S5* does not affect exchange in the *b-pr* region but these data are not, of course, conclusive. However, were *S5* to be a duplication for *Su(H)*$^{+}$, its lethality with *Su(H)*$^{-}$ deletions and other *l(2)br7* alleles would not be expected: Table 7 shows that these are *not* properties of other duplications that include this locus, although the lethality of *Su(H)* with *Dp(2;2)Sco*$^{R+17L}$*C158.1*^{R} is unexpected. Neither parental inversion is lethal with *Su(H)*.

DISCUSSION

Lethal alleles of *l(2)br7* act as dominant suppressors of Hairless; all except *BMW4* do so to approximately the same extent, adding between seven and ten bristles per fly. Deficiencies that include *l(2)br7* have a similar phenotypic effect. These data suggest that *Su(H)* and its suppressor alleles are amorphic alleles. This conclusion is strengthened by the properties of *BMW4*—an allele of *Su(H)* that is clearly leaky with respect to its lethal phenotype. It is also a weaker suppressor of *H* than any of the strong lethal alleles.

On the other hand, the degree of enhancement of the Hairless phenotype that results from both *S5* and duplications covering the *l(2)br7* region are also very similar, producing an extra loss of 12 to 13 bristles per fly. This suggests that *S5* is a hypermorphic, ("overproducing") allele or a very small duplication of the wild-type allele. If this is so, the relative rarity of dominant enhancer alleles, compared to the frequency of dominant suppressor alleles (*i.e.*, 1 : 11) is

TABLE 6

Effects of duplications for region 35 on the expression of H*

	Dp			*Cy*			
	n	$\bar{x}$	*s.e.*	n	$\bar{x}$	*s.e.*	Difference
Dp(2;2)Adh3	20	32.50	0.40	20	29.20	0.47	+ 3.30
Dp(2;2)C163.41^{L}C158.1^{R}	20	13.85	0.33	20	26.75	0.57	—12.90
Dp(2;2)Sco^{R+17L}C158.1^{R}	10	14.70	1.20	10	27.90	1.24	—13.20
Df(2L)C158.1^{L}Sco^{R+17R}	33	35.88	0.30	40	31.71	0.43	+ 4.17†
Dp(2;2)GYS	20	16.45	0.72	20	28.00	0.84	—11.55
Dp(2;2)GYL	20	21.67	0.58	20	30.60	0.59	— 8.93
Dp(2;1)Sco^{R+23}/+; +/+	20	17.25	0.15	20	28.60	0.43	—11.35‡
Dp(2;1)Sco^{R+23}/+ or *Y*; *CyO*/+	40	17.10	0.16		—		—11.52
Dp(2;1)Sco^{R+23}/+ or *Y*; *Df(2L)Sco^{R+23}*/+		—		40	28.62	0.39	
Dp(2;1)Sco^{R+23}/Dp(2;1)Sco^{R+23}; +/+	38	9.89	0.28		—		— 9.19
Dp(2;1)Sco^{R+23}/Y; +/+	40	19.08	0.39		—		
Dp(2;1)Sco^{R+23}/+; *S5*/+	20	7.10	0.45		—		— 8.00
Dp(2;1)Sco^{R+23}/+; *Cy*/+		—		20	15.10	0.40	

* Bristles were counted on *Dp*/+; *Gl Sb H*/+ and *Cy*/+; *Gl Sb H*/+ siblings (except in the case of *Dp(2;2)C158.1^{L}Sco^{R+17R}* when the balancer was *In(2LR)Gla*).

† The suppression of *H* by this deficiency is low since the *Df(2L)C158.1^{L}Sco^{R+17R}* chromosome itself has about two bristles per fly less than wild type, as it is a Scutoid revertant.

‡ The controls for these data were +/+; +/+; *Gl Sb H*/+ male siblings from the cross of *Dp(2;1)Sco^{R+23}*/*Y*; +/+; +/+ males to +/+; +/+; *Gl Sb H*/*In(3L+3R)P* females.

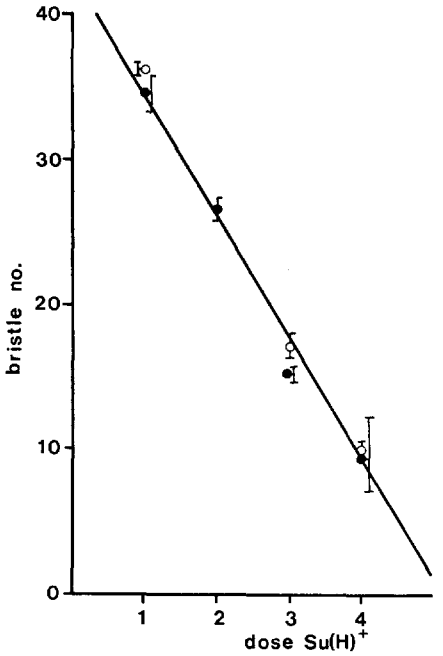

FIGURE 2.—The relationship between bristle number of $H^1/+$ flies and the number of doses of the $l(2)br7^+$ allele. $l(2)br7^+/-$ data: open circle, mean (± *s.e.*) of 12 counts of various $l(2)br7/+$ genotypes. $l(2)br7^+/l(2)br7^+$ data, mean (+ s.e.) of 52 control genotypes. $l(2)br7^+/l(2)br7^+/l(2)br7^+$ data, open circle, mean (± *s.e.*) of 11 different counts of $Dp(2)br7^+/+$, closed circle, mean (± *s.e.*) of 13 different counts of $l(2)br7^{S5}/+$. $l(2)br7^+/l(2)br7^+/l(2)br7^+/l(2)br7^+$, open circle, mean (and range) of two different counts of $Dp(2;1)Sco^{R+23}/Dp(2;1)Sco^{R+23};+/+$, closed circle, mean (and range) of two different counts of $Dp(2;1)Sco^{R+23}/+$; $l(2)br7^{S5}/+$. Line fitted by eye.

understandable, since the commonest consequence of mutation would be expected to be a loss of function. The fact that *S5* is lethal with the suppressor alleles makes it unlikely that this is simply a small $l(2)br7^+$ duplication.

A consequence of the discovery of dominant enhancers of Hairless that are not overt duplications is that this phenotype cannot, by itself, be used as a criterion for duplications in region 35.

TABLE 7

The viability of $1(2)br7^{Su(H)}$ *and* $1(2)br7^{S5}$ *with* $1(2)br^7+$ *duplications*

	Su(H)	*S5*
$C163.41^LC158.1^R/CyO$	297/747	158/425
$Sco^{R+17L}C158.1^R/Gla$	0/131	78/295
Dp(2;2)GYL/CyRoi	194/574	151/373
$Dp(2;1)Sco^{R+23}/Dp(2;1)Sco^{R+23}$; +/+	60/307	136/320

* Number of *l(2)br7/Dp* progeny over total progeny. Duplication carrying females (left hand column) were crossed to *Su(H)/CyO* or *S5/CyO* males.

The nature of the interaction between *l(2)br7* and *H* remains, in molecular terms, as enigmatic as ever. Formally the H^+ and $l(2)br7^+$ products could act antagonistically on a process involved in bristle development. Hairless is haploinsufficient (LINDSLEY *et al.* 1972) and almost recessive in $H/H^+/H^+$ triploids (GOWEN 1933). If, as these data suggest, Hairless is an amorph, then the wild type "balance" between the $H^+$and $l(2)br7^+$ products could be restored in *H* flies by mutation of $l(2)br7^+$ to an amorphic or hypomorphic allele or by deletion of one wild-type *l(2)br7* locus. Conversely, mutation of $l(2)br7^+$ to an allele that produces a greater amount of its product, or its duplication, would result in an enhanced antagonism and a more severe Hairless phenotype. A simple version of this hypothesis (Figure 3) is that $l(2)br7^+$ and H^+ act sequentially during development, the product of $l(2)br7^+$ being the substrate for the H^+ reaction. The accumulation of the intermediate (*i.e.*, the $l(2)br7^+$ product) that would result from mutation of H^+ to *H* would, in that case, be responsible for the *H* phenotype. This accumulation would be relieved by mutation of *l(2)br7* to a less active allele but aggravated by its mutation to a more active allele or its duplication.

This scheme is not entirely satisfactory because it disregards the fact that *l(2)br7* alleles do not affect the recessive lethality of *H* alleles; nor does it account for the lethality of heterozygotes between suppressor and enhancer alleles of *l(2)br7*.

Another example of allelic enhancers and suppressors may be *Su(S)* and *E(S)*. Deficiencies for the region between the distal breakpoints of *In(2L)Cy* and *In(2L)t* (*i.e.*, Df(2L)22D1.2;22D3-E1) act as dominant suppressors of Star. LEWIS (1945) indicated that the reciprocal exchange product, that is, the duplication for the same region, enhanced the expression of Star. A dominant enhancer of Star (*E(S)*) is known, but since it occurred on *In(2L)Cy* its precise genetic relationship to the region between the *In(2L)Cy* and *In(2L)t* breakpoints is unclear.

The Medical Research Council of London is thanked for financial support for this work, which forms part of the genetic analysis of the *Adh* region of the Drosophila genome. I thank E. H. GRELL, HANS GLOOR, SYDNEY AARON, W. SOFER and GEORGE YANNOPOULOS for stocks;

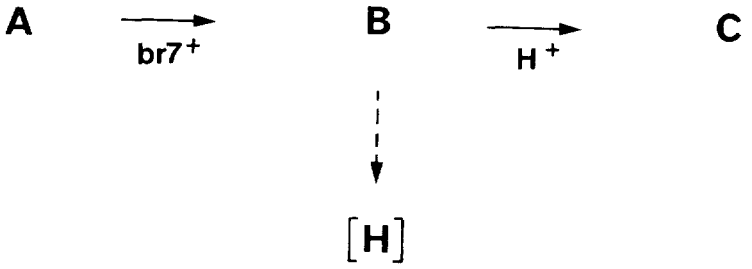

FIGURE 3.—A simple model for Hairless: *A* is the substrate for the $Su(H)^+$ reaction; *B* is its product, which serves as the substrate for the H^+ reaction. The accumulation of *B* results in the *H* phenotype (*H*), which will be relieved by mutation of $Su(H)^+$ to an amorphic allele but enhanced by mutation to a hypermorphic allele.

and my colleague D. GUBB for the *Df(2L)TE36* deficiencies. I also thank R. C. WOODRUFF for help in the early stages of this work and TREVOR LITTLEWOOD, PAM ANGEL and GLYNNIS HARRINGTON for excellent technical help.

LITERATURE CITED

AARON, C. S., 1979 X-ray induced mutations affecting the level of the enzyme alcohol dehydrogenase in *Drosophila melanogaster*: Frequency and genetic analysis of null-enzyme mutants. Mutation Research **63:** 127–137.

BRIDGES, C. B. and T. H. MORGAN, 1923 The third-chromosome group of mutant characters of *Drosophila melanogaster*. Carnegie Institute of Washington. Pub. 327. 251 pp.

GOWEN, J. W., 1933 Constitutional effects on the Hairless gene in diploid and triploid *Drosophila*. Amer. Nat. **67:** 178–180.

HENIKOFF, S., 1980 A more conventional view of the "ebony" gene. Dros. Inf. Service **55:** 61-62.

KAUFMAN, T. C., S. E. TASAKA and D. J. SUZUKI, 1973 The interaction of two complex loci, *zeste* and *bithorax* in *Drosophila melanogaster*. Genetics **75:** 299–321.

LEWIS, E. B., 1945 The relation of repeats to position effect in *Drosophila melanogaster*. Genetics **30:** 137–166.

LINDSLEY, D. L. and E. H. GRELL, 1968 Genetic variations of *Drosophila melanogaster*. Carnegie Inst. Washington Pub. 627. 427 pp.

LINDSLEY, D. L., L. SANDLER, B. S. BAKER, A. T. CARPENTER, R. E. DENELL, J. C. HALL, P. A. JACOBS, G. L. C. MIKLOS, P. A. DAVIS, R. C. GETHMANN, R. W. HARDY, A. HESSLER, S. M. MILLER, H. NOZAWA, D. M. PARRY and M. GOULD-SOMERO, 1972 Segmental aneuploidy and the genetic gross structure of the Drosophila genome. Genetics **71:** 157–184.

NASH, D., 1970 The mutational basis for the "allelic" modifier mutants, *Enhancer* and *Suppressor of Hairless*, of *Drosophila melanogaster*. Genetics **64:** 471–499.

O'DONNELL, J., H. C. MANDEL, M. KRAUSS and W. SOFER, 1977 Genetic and cytogenetic analysis of the Adh region in *Drosophila melanogaster*. Genetics **86:** 553–566.

PLUNKETT, C. R., 1926 The interaction of genetic and environmental factors in development. J. Exp. Zool. **46:** 181–244.

VAN BREUGEL, F. M. A., A. RAY and H. GLOOR, 1968 A comparison of banding patterns in salivary gland chromosomes of two species of *Drosophila*. Genetica **39:** 165–192.

WOODRUFF, R. C. and M. ASHBURNER, 1979a The genetics of a small autosomal region of *Drosophila melanogaster* containing the structural gene for alcohol dehydrogenase. I. Characterization of deficiencies and mapping of *Adh* and visible mutations. Genetics **92:** 117–132. ——, 1979b II. Lethal mutations in the region. Genetics **92:** 133–149.

YANNOPOULOS, G., N. STAMATIS, A. ZACHAROPOULOU and M. PELECANOS, 1981 Differences in the induction of specific deletions and duplications by two male recombination factors isolated from the same *Drosophila* natural population. Mutation Research **83:** 383–393.

Corresponding editor: T. C. KAUFMAN