*Proc. Natl. Acad. Sci. USA*
Vol. 79, pp. 7380–7384, December 1982
Developmental Biology

# Genes controlling segmental specification in the *Drosophila* thorax

(homeosis/insect segments/determination/clonal analysis)

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*Communicated by M. F. Perutz, August 25, 1982*

**ABSTRACT** **The roles of three homeotic genes, *Ubx*$^+$, *Scr*$^+$, and *Antp*$^+$, in the *Drosophila* thorax have been studied by determining the cellular phenotypes of mutations resulting in loss of gene function. The principal results are: (*i*) The *Scr*$^+$ and *Ubx*$^+$ genes are required in the prothorax and metathorax, respectively; in the absence of these genes, both segments develop like the mesothorax. (*ii*) The *Antp*$^+$ gene is required in all three thoracic segments: in its absence, parts of the mesothorax are transformed into corresponding parts of the antenna, and similar transformations to antenna are found in the prothorax and metathorax if the *Scr*$^+$ and *Ubx*$^+$ genes also are absent. (*iii*) Loss of the *Ubx*$^+$ gene early in embryogenesis, but not later, leads to the inappropriate activity of the *Scr*$^+$ gene in the meso- and metathorax. Results *i* and *ii* argue strongly that segmental determination is specified in a combinatorial fashion in the head and thorax by the selective activities of the *Scr*$^+$, *Ubx*$^+$, *Antp*$^+$, and putative head-determining genes. Result *iii* suggests that a product of the *Ubx*$^+$ gene also plays an early, regulatory role in ensuring the correct spatial expression of the *Scr*$^+$ gene during subsequent development.**

Insects are composed of a series of head, thoracic, and abdominal segments, each displaying unique and sometimes dramatically different characteristics. Yet, in the absence of particular homeotic genes, one or more segments can be transformed into other segments (1–4). Thus, segments are homologous units in which diverse cell patterns develop under discrete genetic controls.

Of the many homeotic genes that have been described in *Drosophila*, several have the distinguishing feature that they must be active in some segments and inactive in others [e.g., genes of the bithorax-complex (1, 2) and the *Antp*$^+$ (5–7) and *Scr*$^+$ (8–10, 6) genes]. Such segment-specific genes appear to dictate the particular developmental pathways followed by the different segments. Recently, a second class of homeotic genes has been identified whose members appear to be required in most, or all, segments. The products of two of these genes [*Pc*$^+$ (2, 11) and *esc*$^+$ (12)] appear to be required for the selective expression of the bithorax-complex genes and possibly other segment-specific genes. Thus, these gene products may have regulatory roles in ensuring the correct expression of segment-specific homeotic genes.

In this report I describe the interdependent roles of three segment-specific homeotic genes (*Ubx*$^+$, *Antp*$^+$, and *Scr*$^+$) in the cells giving rise to the adult thorax of *Drosophila*. The results argue strongly that these genes act in a combinatorial fashion to specify segmental determination. In addition, they suggest that the products of some of these genes also have regulatory roles in controlling the selective expression of others.

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## METHODS

**Genotypes Employed.** Except where otherwise indicated, all mutations and chromosomes are described in ref. 13. The *Ubx*$^1$ mutation behaves as a hypomorph, resulting in the loss of most, but probably not all, of the wild-type gene function (14, 15). The *Antp*$^{Ns+RC3}$ mutation is an apparent null allele of the *Antp*$^+$ gene (7). The *Scr*$^{13A}$ mutation is a recessive lethal allele kindly provided by C. Nüsslein-Volhard. The *Scr*$^{C1}$ mutation was induced on a chromosome already bearing the *Antp*$^{NS+RC3}$ mutation with the mutagen ethyl methanesulfonate (unpublished data). Both the *Scr*$^{13A}$ and *Scr*$^{C1}$ mutations cause embryonic lethality when *trans* to other *Scr* mutations; also, such mutant embryos show the characteristic homeotic phenotype resulting from loss of the *Scr*$^+$ gene described previously (6).

**Analysis of Mutant Clones.** Marked clones of cells homozygous for mutations of the *Scr*, *Antp*, and *Ubx* loci were obtained as described below for the triple mutant combination *Scr*$^{C1}$ *Antp*$^{Ns+RC3}$ *Ubx*$^1$. A chromosome carrying all three mutations as well as the *e*$^{11}$ mutation was constructed, and embryos or larvae of the genotype *Scr*$^{C1}$ *Antp*$^{Ns+RC3}$ *Ubx*$^1$ *e*$^{11}$/*Ki Sb*$^{63b}$ *M(3)w*$^{124}$ were irradiated at appropriate times after egg laying (3 ± 1 hr = blastoderm stage and 24–48 hr = first larval instar; all experiments were performed at 25°C). All the mutations are located on the right arm of the third chromosome; because *Ki* is positioned closest to the centromere, mitotic recombinations that occur between *Ki* and the centromere can give rise to homozygous *Ki*$^+$ *Sb*$^+$ *M(3)w*$^+$ cells, which must also be homozygous for the *Scr*$^{13A}$, *Antp*$^{Ns+RC3}$, *Ubx*$^1$, and *e*$^{11}$ mutations. The *Kinked*, *Stubble*$^{63b}$, and *Minute(3)w*$^{124}$ mutations are dominant and affect bristle morphology; the *ebony*$^{11}$ mutation is recessive and causes cuticle, especially bristles, to be heavily pigmented. Thus, clones of homozygous cells bear blackened, but otherwise normal, bristles, in contrast to surrounding heterozygous cells that bear gnarled, stunted bristles. In addition to affecting bristle morphology, the *M(3)w*$^{124}$ mutation also causes heterozygous cells to divide at slower than normal rates (16). Consequently, homozygous *Ki*$^+$ cells carrying two copies of the *M(3)w*$^+$ allele are able to grow faster than surrounding heterozygous cells (17) and hence, can form large portions of the adult compartments (18) to which they contribute.

Clones were identified either under the dissecting or compound microscope by the appearance of marked bristles and because they frequently disrupted the normal morphology. Clones in several parts of the fly that normally carry few, or no, large bristles were difficult to detect and hence, may have been missed. In addition, because of the large numbers of flies involved (*ca.* 15,000), it was not possible to screen all parts of all flies with equal thoroughness. For these reasons, the frequencies of clones in different parts of the fly, or of clones of different

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genotypes in the same part, cannot be usefully compared.

All clones identified under the dissecting microscope were subsequently examined under the compound microscope.

## RESULTS

The independent roles of the *Ultrabithorax*$^+$ (*Ubx*$^+$) and *Antennapedia*$^+$ (*Antp*$^+$) genes have been studied previously by inducing marked clones of cells homozygous or hemizygous for mutations of either locus (e.g., *Ubx*$^1$ and *Antp*$^{Ns+RC3}$) in embryos or larvae that are otherwise heterozygous (1, 7, 15, 19). Here, this approach has been applied to the *Sex combs reduced*$^+$ (*Scr*$^+$) gene (8–10) and to all possible combinations of the *Antp*$^+$, *Scr*$^+$, and *Ubx*$^+$ genes by generating marked clones of the following mutant genotypes: *Scr*$^{13A}$, *Scr*$^{C1}$ *Antp*$^{Ns+RC3}$, *Scr*$^{13A}$ *Ubx*$^1$, *Antp*$^{Ns+RC3}$ *Ubx*$^1$, and *Scr*$^{C1}$ *Antp*$^{Ns+RC3}$ *Ubx*$^1$. The phenotypes of such clones are summarized in Table 1, illustrated in Fig. 1, and described below.

***Ubx*$^1$ Clones.** Clones induced after 8 hr following fertilization are normal in the pro- and mesothoracic segments but transform the dorsal and ventral appendages of the metathorax (haltere and third leg) into their counterparts in the mesothorax (wing and second leg) (1, 15, 19). Clones induced earlier are identical except that they transform the posterior compartments of both the second and third legs into the posterior compartment of the first leg (refs. 15 and 20; e.g., Fig. 1). Thus, the *Ubx*$^+$ gene is required in the metathorax to specify meta- as opposed to mesothoracic development. In addition, it appears to have an early function in portions of the posterior meso- and metathorax in preventing prothoracic development.

***Scr*$^{13A}$ Clones.** The *Scr*$^+$ gene, which maps close to the *Antp*$^+$ gene, has been defined by a series of dominant and recessive mutations (8–10). Though most of these mutations result in lethality when homozygous, one mutant allele, *Scr*$^{EdR18}$, is viable when *trans* to other recessive mutations of the gene; such mutant flies show transformations of the first leg to second leg and of the proboscis to maxillary palp, but the meso- and metathoracic segments are normal (10). Clones of cells homozygous for the *Scr*$^{13A}$ mutation were induced around the blastoderm stage or during subsequent development. These clones are normal in both the meso- and metathoracic segments but cause autonomous transformation of all portions of the first leg into corresponding portions of the second leg (Fig. 1). A few *Scr*$^{13A}$ clones were observed in the dorsal derivative of the prothorax, the humerus. However, these clones were small, marking one, or at most a few bristles, and hence, difficult to interpret. Finally, clones in the proboscis autonomously transformed the labial palps into maxillary palps, but clones in the eye-antenna were normal. These results indicate that the *Scr*$^+$ gene is not required either in the meso- or metathorax or in the eye-antenna but that it is required in at least the ventral prothorax for specifying pro- as opposed to mesothoracic development. In addition, they indicate that the *Scr*$^+$ gene is required in the proboscis for specifying labial as opposed to maxillary development.

***Scr*$^{13A}$ *Ubx*$^1$ Clones.** The phenotype of *Scr*$^{13A}$ *Ubx*$^1$ clones induced around the blastoderm stage and during larval development is the additive phenotype of *Scr*$^{13A}$ and *Ubx*$^1$ clones induced during larval development (Fig. 1). Thus, in the thorax, doubly mutant cells transform the pro- and metathorax into mesothorax but do not affect the mesothorax itself. This result indicates that the transformation of portions of the meso- and metathorax to prothorax caused by early loss of the *Ubx*$^+$ gene (15, 20) only occurs if the *Scr*$^+$ gene is present and hence, suggests that this transformation results from the expression of the *Scr*$^+$ gene in the meso- and metathorax where it should normally be inactive.

Table 1. Phenotypes and numbers of mutant clones

| Genotype† and time of clone induction, hr | Phenotype‡ and number§ | | | | | | | Flies, no. | X-ray dose, rads¶ |
|---|---|---|---|---|---|---|---|---|---|
| | Eye-antenna | Proboscis | Leg 1 Ant.:Post. | Leg 2 Ant.:Post. | Leg 3 Ant.:Post. | Wing | Haltere | | |
| ***wild type*** | **EA** | **P** | **1** | **2** | **3** | **W** | **H** | — | — |
| ***Ubx:*** 4 ± 2 | **EA** | **P** | **1** | **2:1*** | **2:1*** | **W** | **W** | Refs. 15, 20 | |
| ***Ubx:*** 48 ± 4 | **EA** | **P** | **1** | **2** | **2** | **W** | **W** | Refs. 15, 19, 20 | |
| ***Scr*** | **EA** | **M** | **2** | **2** | **3** | **W** | — | | |
| 3 ± 1 & 48 ± 4 | 45 | 25 | 27:13 | 60:9 | 33:13 | 21 | — | 4,280 | 750, 1,000 |
| ***Scr Ubx*** | **EA** | **M** | **2** | **2** | **2** | **W** | **W** | | |
| 3 ± 1 | 5 | 2 | 5:12 | 22:23 | 20:15 | 8 | 10 | 2,325 | 750 |
| 48 ± 4 | 13 | 4 | 7:3 | 19:7 | 13:1 | 36 | 6 | 1,500 | 1,000 |
| ***Antp*** | **EA** | **P** | **(1)** | **A*** | **(3)** | **(W)** | — | | |
| 3 ± 1 & 24–48 | 61 | 23 | 7(13):33(40) | 49(64):27(31) | 16(27):4(10) | 10(18) | — | 3,090 | 500, 1,000 |
| ***Scr Antp Ubx*** | **EA** | **M** | **A*** | **A*** | **A*** | **(W)** | **W** | | |
| 3 ± 1 & 48 ± 4 | 64 | 16 | 15:12 | 30(35):11 | 30(41):17 | 11(20) | 24 | 2,200 | 500, 1,000 |
| ***Antp Ubx*** | **EA** | — | **(1)** | **A*** | **A*** | **(W)** | **W** | | |
| 3 ± 1 | 1 | — | 1(2):0 | 2:2 | 5:0 | 0 | 0 | 250 | 750 |
| 48 ± 4 | 12 | — | 3(9):2(5) | 11(12):9 | 15:2 | 2 | 14 | 475 | 1,000 |
| ***Scr Antp*** | **EA** | **M** | **A*** | **A*** | **(3)** | **(W)** | — | | |
| 3 ± 1 & 48 ± 4 | 18 | 1 | 10:5 | 4(8):1 | 2(3):0(2) | 3(6) | — | 1,400 | 750, 1,000 |

† Genotypes are shown in **boldface**; time of clone induction (hours after egg laying) is given in standard type underneath. Full genotypes are given in *Results*.

‡ Phenotypes are shown in **boldface**. Ant. and Post. refer to the anterior and posterior compartments of the legs which are treated separately when they differ in phenotype. **1*** = prothoracic pattern formed in proximal posterior leg instead of mesothoracic pattern. **A*** = antennal structures or antennal and mesothoracic structures formed. Parentheses [e.g., **(W)**] = abnormal or abbreviated cuticular patterns formed. **M** = maxillary tissue formed instead of labial tissue in the proboscis.

§ Numbers of clones having the phenotype shown in **boldface** are given in standard type underneath. Clones in the anterior and posterior compartments of the legs are treated separately. Numbers in parentheses indicate total numbers of clones when only some of the clones showed the phenotype indicated in **boldface** and the remainder appeared normal.

¶ One rad = 0.01 gray.

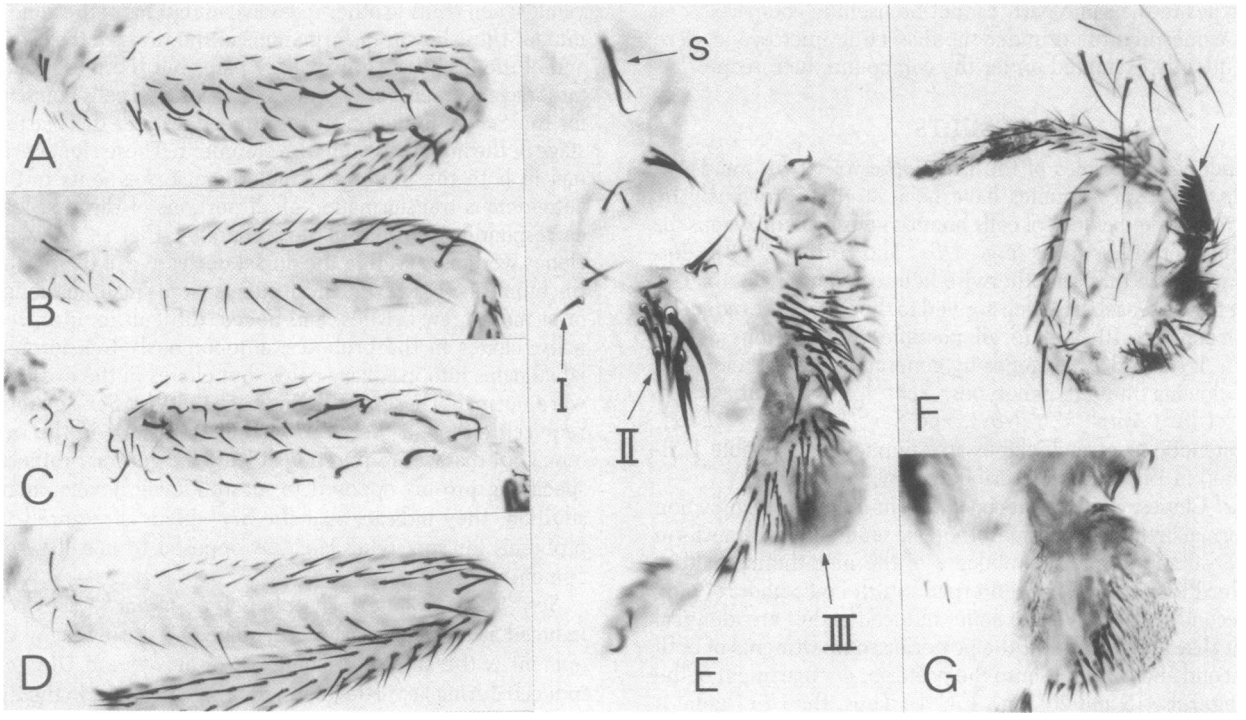


FIG. 1. Phenotypes of mutant clones. (*A–D*) Sibling $Ubx^1$ and $Scr^{13A}$ $Ubx^1$ clones induced in the posterior compartments of the first and second legs around the blastoderm stage (mitotic recombination in $Scr^{13A}$ $Ubx^1$ $e^{11}$/*Ki* $Sb^{63b}$ $M(3)w^{124}$ cells can give rise to $Scr^{13A}$ $Ubx^1$ clones if it occurs proximal to the *Ki* locus or to Kinked $Ubx^1$ clones if it occurs distal to the *Scr* locus). (*A*) Kinked $Ubx^1$ clone in the posterior femur of the first leg showing the normal bristle pattern. (×80.) (*B*) $Scr^{13A}$ $Ubx^1$ clone in the posterior femur of the first leg that forms the bristle pattern normally found in the posterior femur of the second leg (compare with *D*). (×80.) (*C*) Kinked $Ubx^1$ clone in the second leg that forms the bristle pattern normally found in the first leg (compare with *A*). (×80.) (*D*) $Scr^{13A}$ $Ubx^1$ clone in the second leg forming the normal bristle pattern. (×80.) (*E*) $Scr^{C1}$ $Antp^{Ns+RC3}$ $Ubx^1$ clone induced in the anterior compartment of the first leg during the late first instar. In addition to normal second leg structures (e.g., s, the sternopleura bristles), this clone also forms tissue characteristic of the first (I), second (II), and third (III) antennal segments. (×150.) (*F*) $Antp^{Ns+RC3}$ $Ubx^1$ clone induced in the anterior compartment of the first leg around the blastoderm stage. This clone forms an abnormal pattern of bristles and is associated with fusion of the femur and tibia. The remainder of the clone forms normal structures in the proximal and distal portions of the leg, including the sex comb (arrow). (×100.) (*G*) Detail of the clone in *E* showing sensilla characteristic of the normal third antennal segments. (×200.)

**$Antp^{Ns+RC3}$ Clones.** The phenotype of homozygous $Antp^{Ns+RC3}$ clones has been described (7). Whether induced around the blastoderm stage or during larval development, such clones transform portions of the second leg (both anterior and posterior compartments) into corresponding portions of the antenna. However, some portions of the leg, notably the distal tarsus, develop normally even when mutant. Some clones in the wing and mesonotum as well as in the first and third legs show abnormal or abbreviated patterns of bristles, but others appear normal (Table 1; Fig. 1). Finally, all clones in the head are normal. These results led to the conclusion that the $Antp^+$ gene is required in all three thoracic segments, though only in the ventral second leg could the gene be said to be required for specifying one determined state (mesothorax) as opposed to another (eye-antenna) (7).

**$Scr^{C1}$ $Antp^{Ns+RC3}$ $Ubx^1$ Clones.** The phenotype of triply mutant cells induced either around the blastoderm stage or during subsequent development is the additive phenotype of $Antp^{Ns+RC3}$ and $Scr^{13A}$ $Ubx^1$ clones—i.e., such clones transform corresponding portions of all three legs into antennal structures (as in $Antp^{Ns+RC3}$ clones in the second leg), whereas remaining portions of these legs, which are not transformed into antenna, develop as in the mesothorax (Fig. 1). The phenotypes of triply mutant cells in the wing and mesonotum are indistinguishable from that of equivalent $Antp^{Ns+RC3}$ clones; triply mutant cells in the haltere and metanotum formed wing and mesonotum structures. Finally, $Scr^{C1}$ $Antp^{Ns+RC3}$ $Ubx^1$ clones were completely normal in the eye-antenna but transformed the labial palps of the proboscis into maxillary palps. These results suggest that the $Antp^+$ gene is required in all three thoracic segments for specifying one determined state (mesothorax) as opposed to another (eye-antenna) but that this requirement is obscured in the pro- and metathorax by the activities of the $Scr^+$ and $Ubx^+$ genes.

**$Scr^{C1}$ $Antp^{Ns+RC3}$ Clones.** $Scr^{C1}$ $Antp^{Ns+RC3}$ clones induced in the head and pro- and mesothorax during embryonic and larval development were indistinguishable in phenotype from triply mutant clones induced in the same segments. Clones induced in the metathorax were indistinguishable from $Antp^{Ns+RC3}$ clones in the metathorax.

**$Antp^{Ns+RC3}$ $Ubx^1$ Clones.** $Antp^{Ns+RC3}$ $Ubx^1$ clones induced in the meso- and metathorax during larval development were indistinguishable in phenotype from triply mutant clones induced in the same segments. Clones induced in the head and prothorax were indistinguishable from $Antp^{Ns+RC3}$ clones in the head and prothorax (Fig. 1). Clones induced at the blastoderm stage behaved like clones induced during larval development with one curious exception. One of the two clones obtained in the posterior compartment of the second leg differentiated prothoracic structures in the proximal leg and antennal structures in the distal leg. Normally, $Antp^{Ns+RC3}$ clones are able to transform only the second leg into antenna. Hence, the distal portion of this clone behaved like an $Antp^{Ns+RC3}$ clone in the distal second leg, even though the proximal portion differentiated prothoracic structures. This result suggests that $Ubx^1$ clones induced around the blastoderm stage may transform only proximal portions of the posterior second leg into corresponding portions of the first leg.

## DISCUSSION

The principal results to be considered are: (*i*) The prothorax and metathorax require the activities of the $Scr^+$ and $Ubx^+$ genes, respectively, throughout development; in the absence of both genes, both segments develop like the mesothorax. (*ii*) All three thoracic segments require the activity of the $Antp^+$ gene. In the absence of this gene, part of the mesothorax is transformed into corresponding antennal structures, and similar transformations to antenna are observed in the prothorax and metathorax when the $Scr^+$ and $Ubx^+$ genes also are absent. (*iii*) Loss of the $Ubx^+$ gene early in development, but not later, causes posterior portions of the meso- and metathorax to develop as in the prothorax (15, 20). This phenotype is only observed when the $Scr^+$ gene is present.

Result *i* provides further evidence for the view (1, 2, 4, 7) that the mesothorax is an epigenetic ground state in which none of the segment-determining genes either is active or required and that the more specialized segments of the head, thorax, and abdomen are elaborations of this ground state specified by the activities of homeotic genes. In contrast, results *ii* and *iii* indicate that both the $Antp^+$ and $Ubx^+$ genes are required for mesothoracic development and hence, challenge this hypothesis.

The concept of a ground state has been useful in interpreting the phenotypes of many homeotic genes (1, 2, 4, 7). Moreover, it makes good sense in evolutionary terms, because insects almost certainly arose from more primitive, millipede-like ancestors composed mostly of similar leg-bearing segments (21–23). Therefore, instead of discarding this concept, I suggest the following, more complex interpretation of the *Ubx* and *Antp* phenotypes. In the case of the *Ubx* phenotype, result *iii* suggests that the $Ubx^+$ gene may be required in the posterior mesothorax only for preventing the $Scr^+$ gene from being expressed inappropriately. This suggestion is supported by result *i*, because in the absence of both the $Ubx^+$ and $Scr^+$ genes, the mesothorax develops normally. A similar argument has been made for the role of the $Antp^+$ gene: assuming that the eye-antenna segment

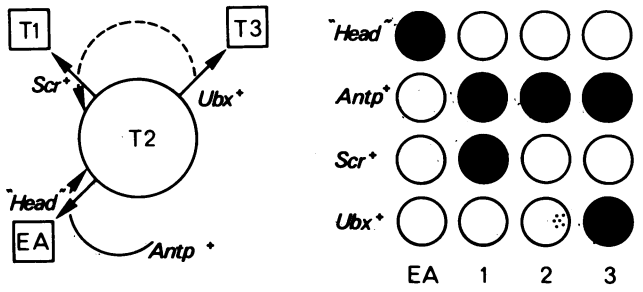


FIG. 2. Proposed roles (*Left*) and realms of action (*Right*) of the $Antp^+$, $Scr^+$, and $Ubx^+$ genes. The prothorax (T1), metathorax (T3), and eye-antenna (EA) of the adult fly are elaborations of the ground state mesothorax (T2) specified by the continuous activities of the $Scr^+$, $Ubx^+$, and putative head-determining genes, respectively (shown as arrows leading from T2 to T1, T3, and EA) during embryonic and larval development. In addition to its role in specifying metathoracic development, the $Ubx^+$ gene also encodes a product that has a transient early role (15, 20) in preserving the ground state by preventing inappropriate activity of the $Scr^+$ gene or gene product during subsequent development [curved arrow (broken line) blocking the activity of the $Scr^+$ gene]. Similarly, the $Antp^+$ gene product is required to preserve the ground state by preventing inappropriate activity of the head-determining genes or gene products [curved arrow (solid line) blocking the activity of the head-determining genes], though unlike the $Ubx^+$ gene product, it appears to be required continuously (7). The realms of action of the $Antp^+$, $Scr^+$, $Ubx^+$, and "*Head*" genes in the eye-antenna and thoracic segments (1, 2, 3) are indicated in matrix form, each row representing a gene and each column representing a segment. Closed circles, gene product must be active in at least part, if not all, of the segment. Open circles, gene product must be absent or inactive. Circles with dots, gene product must be active early but is absent or inactive subsequently.

is an elaboration of the ground state specified by one or more head-determining genes, the phenotypes of dominant and recessive mutations of the $Antp^+$ gene suggest that it is required in ventral portions of the mesothorax only to prevent inappropriate activity of the head-determining genes or their products

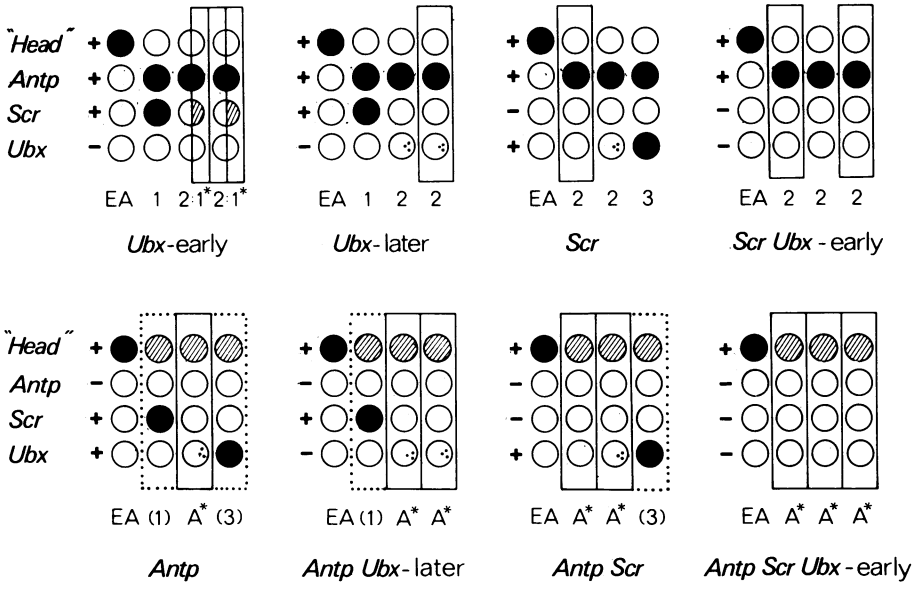


FIG. 3. Combinatorial roles of the $Antp^+$, $Scr^+$, $Ubx^+$, and putative head-determining genes in specifying segmental determination in the thorax and eye-antenna. The genetic and phenotypic consequences of removing these genes singly or in combination are diagramed in matrix form as in the wild-type case shown in Fig. 2 (lightly shaded circles and half circles indicate inappropriate activity of gene product; full descriptions of phenotypes are given in *Results* and Table 1 and full genotypes are given in *Results*). Segments in which gene loss has no effect on the code word of active and inactive gene products develop normally and are not boxed; segments in which gene loss results in an inappropriate code word are homeotically transformed (boxes); segments in which a nonsense code word is created develop abnormally (boxes with dotted lines). Early or later times of gene loss are indicated where relevant.

(7). This interpretation predicts that in the absence of both the $Antp^+$ and head-determining genes, the mesothorax should develop normally. However, this prediction cannot be tested until mutations that inactivate the putative head-determining genes are isolated. In summary, both the $Antp^+$ and $Ubx^+$ genes may act in the mesothorax only as regulatory functions that preserve the ground state by preventing the inappropriate activity of other homeotic genes or their products. According to this hypothesis, the mesothorax should develop normally in the simultaneous absence of the *bithorax*-complex, $Antp^+$, $Scr^+$, and putative head-determining genes and hence, correspond to an epigenetic ground state.

The proposed roles and realms of action of the $Antp^+$, $Scr^+$, $Ubx^+$, and putative head-determining genes are outlined in Fig. 2. As shown in Fig. 3, mutations that cause one segment to express a combination of homeotic gene products normally expressed by another segment result in clear homeotic transformations (e.g., $Ubx^1$, $Scr^{13A}$); however, mutations that generate novel combinations of homeotic gene products not normally found in any segment cause the development of abnormal cell patterns (e.g., $Antp^{Ns+RC3}$ in the pro- and metathorax). These findings argue strongly that segmental determination is specified in a combinatorial fashion—mutations such as $Scr^{13A}$ and $Ubx^1$ resulting in inappropriate code words and the $Antp^{Ns+RC3}$ mutation sometimes resulting in nonsense code words. *A priori* it is not possible to predict the phenotypic consequences of a nonsense code word. However, as in the case of the $Antp^{Ns+RC3}$ mutation in the pro- and metathorax, it may be possible to convert a nonsense word into a sense word by eliminating other homeotic genes ($Scr^+$ or $Ubx^+$), thereby leading to a predictable homeotic phenotype.

It has been convenient to classify homeotic genes involved in segmental determination into two groups: (*i*) "selector" genes (24) that specify segmental determination throughout development [e.g., genes of the bithorax-complex (1, 2) and *Antp* (5–7) and *Scr* (6, 8–10) loci] and (*ii*) regulatory genes (2, 11, 25) [e.g., the $Pc^+$ (2, 11) and $esc^+$ (12) genes] that are required in all segments for establishing and maintaining the segment-specific expression of segmental selector genes. However, results *ii* and *iii* challenge this simple classification because they suggest the possibility that the products of some segment-specific selector genes may themselves have regulatory roles in initiating or maintaining the selective expression of other segment-specific genes.

I thank P. A. Lawrence for excellent advice and enthusiastic encouragement throughout this work, C. Nüsslein-Volhard for generously providing the $Scr^{13A}$ mutation, P. Johnston for technical assistance, and several of my colleagues in the Cell Biology Division of the Laboratory of Molecular Biology for critical readings of manuscript. I also thank the Thomas C. Usher Fund and the Medical Research Council of Great Britain for financial support and laboratory facilities.

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