<Further Development 10.10>

Initiation and Maintenance of Homeotic Gene Expression

The initial domains of homeotic gene expression are influenced by the gap genes and pair-rule genes. For instance, expression of the *abdA* and *AbdB* genes is repressed by the gap gene proteins Hunchback and Krüppel. This inhibition prevents these abdomen-specifying genes from being expressed in the head and thorax (Casares and Sánchez-Herrero 1995). Conversely, the *Antennapedia*gene is activated by particular levels of Hunchback (needing both the maternal and the zygotically transcribed messages), so *Antennapedia* is originally transcribed in parasegment 4, specifying the mesothoracic (T2) segment (Wu et al. 2001).

The expression of homeotic genes is a dynamic process. The *Antennapedia* gene, for instance, although initially expressed in presumptive parasegment 4, soon appears in parasegment 5. As the germ band expands, *Antp* expression is seen in the presumptive ventral nerve cord as far posterior as parasegment 12. During further development, the domain of *Antp* expression contracts again, and *Antp* transcripts are localized strongly to parasegments 4 and 5. Like that of other homeotic genes, *Antp* expression is negatively regulated by all the homeotic gene products expressed posterior to it (Levine and Harding 1989; González-Reyes and Morata 1990). In other words, each of the bithorax complex genes represses the expression of *Antp*. If the *Ultrabithorax* gene is deleted, *Antp* activity extends through the region that would normally have expressed *Ubx* and stops where the *Abd* region begins. (This allows the third thoracic segment to form wings like the second thoracic segment, as seen in textbook Figure 10.24.) If the entire bithorax complex is deleted, *Antp* expression extends throughout the abdomen. (Such a larva does not survive, but the cuticle pattern throughout the abdomen is that of the second thoracic segment.)

As we have seen, the proteins encoded by the gap and pair-rule genes are transient; however, in order for differentiation to occur, the identities of the segments must be stabilized. So, once the transcription patterns of the homeotic genes have become stabilized, they are “locked” into place by alteration of the chromatin conformation in these genes. The repression of homeotic genes is maintained by the Polycomb family of proteins, while the active chromatin conformation appears to be maintained by the Trithorax proteins (Ingham and Whittle 1980; McKeon and Brock 1991; Simon et al. 1992).

Realisator genes

Homeotic genes don’t do the work alone. In fact, they appear to regulate the action from up in the “executive suite,” while the actual business of making an organ is done by other genes on the “factory floor.” In this scenario, the homeotic genes work by activating or repressing a group of “realisator genes” that are the targets of the homeotic gene proteins and that function to form the specified tissue or organ primordia (Garcia-Bellido 1975).

Such a pathway for one simple structure—the posterior spiracle—is well on its way to being elucidated. This organ is a simple tube connecting to the trachea and a protuberance called the Filzkörper. The posterior spiracle is made in the eighth abdominal segment and is under the control of the Hox gene *AbdB*. Lovegrove and colleagues (2006) have found that the AbdB protein controls four genes that are necessary for posterior spiracle formation: *Spalt* (*Sal*), *Cut* (*Ct*), *Empty spiracles* (*Ems*), and *Unpaired* (*Upd*). The first three encode transcription factors; the fourth encodes

a paracrine factor. None of them are transcribed without AbdB. Moreover, if these genes are independently activated in the absence of AbdB, a posterior spiracle will form.

Controlled by AbdB, these four regulator genes in turn control the expression of the realisator genes that control cell structure and function. *Spalt* and *Cut* encode proteins that activate the cadherin genes necessary for cell adhesion and the invagination of the spiracle. *Empty spiracles* and *Unpaired* encode proteins that control the small G proteins (such as Gef64C) that organize the actin cytoskeleton and the cell polarizing proteins that control the elongation of the spiracle (Figure 1).

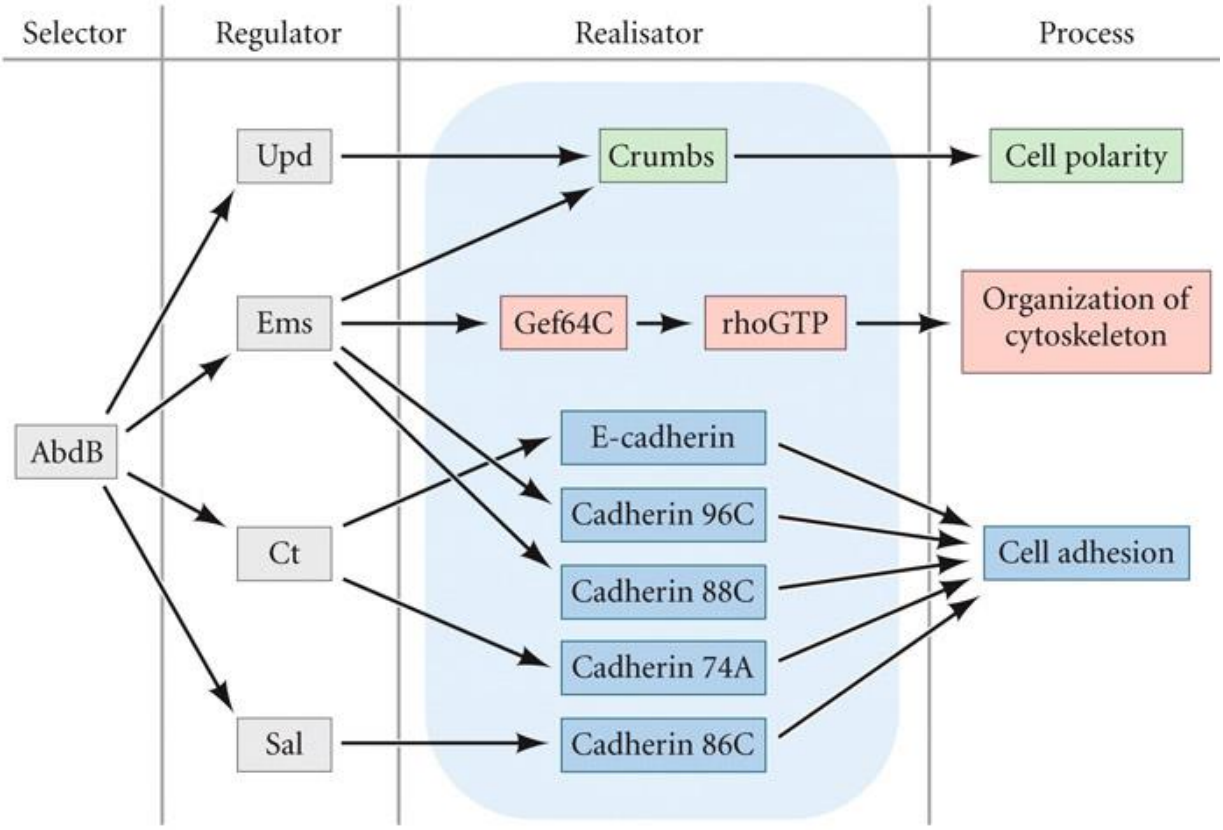

Figure 1 Developmental control of posterior spiracle formation through AbdB. The homeotic selector protein AbdB (with the interaction of cofactors) activates the transcription of four genes encoding "intermediate" regulators. The proteins encoded by these genes—Spalt (Sal), Cut (Ct), Empty spiracles (Ems), and Unpaired (Upd)—are necessary and sufficient for specifying posterior spiracle development. They control (directly or indirectly) the local expression of a battery of realisator genes that influence morphogenetic processes such as cell adhesion (cadherins), cell polarity (Crumbs), and cytoskeletal organization (small G proteins). (After Lohmann 2006; Lovegrove et al. 2006.)

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