plans. Simpson (1944, 1953) and more recently Wallace (1985) strongly attacked Goldschmidt's hypothesis, pointing out that it was not substantiated by knowledge of the nature of the genetic material and that neither the fossil record nor any modern species provided evidence for the instantaneous appearance of totally new structures from one generation to the next. Since patterns of development and adult structures both require extremely close integration of all their component elements and relationships with other aspects of the structure, physiology, and behavior of the organism, it is nearly impossible to conceive of the evolution of new functional complexes occurring through an instantaneous, global restructuring of the genetic material.

Ironically, it is exactly these homeotic mutants that are now providing the strongest evidence of how developmental processes control the body plan of all multicellular organisms. Little more than a decade ago, DNA sequencing showed that **homeotic genes** – a particular family of a larger group of genes termed **homeobox genes** – are characterized by a highly conserved region, the **homeobox**, consisting of 180 bases that code for a particular sequence of amino acids termed the **homeodomain** in regulatory proteins (McGinnis et al. 1984; Scott and Weiner 1984) (Fig. 10.2). The homeodomain serves as a sequence-specific, DNA-binding motif that allows particular proteins to bind to genes that control other aspects of development.

Not only were all homeotic genes in *Drosophila* shown to code for a similar homeodomain, but also comparable genes were recognized among vertebrates and later in all major metazoan phyla (Ruddle et al. 1994a,b; S. Carroll 1995) (Figs. 10.3, 10.4). The conservative DNA sequence of these genes provides an extremely

Figure 10.2. Homeodomain sequences of five proteins encoded by homeobox-containing genes. *Antp, ftz,* and *Ubx* are from *Drosophila; Hox-1* from the mouse; and *MM3* from *Xenopus*. The light boxes enclose homologous sequences, using *Antp* (i.e., *Antennapedia*) as the standard. The invariant sequence in the dark box is the DNA-binding site. From Gehring (1985).

	1																			20
Hox-1	Ser	Lys	Arg	Gly	Arg	Thr	Ala	Tyr	Thr	Arg	Pro	Gln	Leu	Val	Glu	Leu	Glu	Lys	Glu	Phe
MM3	Arg	Lys	Arg	Gly	Arg	Gln	Thr	Tyr	Thr	Arg	Tyr	Gln	Thr	Leu	Glu	Leu	Glu	Lys	Glu	Phe
Antp	Arg	Lys	Arg	Gly	Arg	Gln	Thr	Tyr	Thr	Arg	Tyr	Gln	Thr	Leu	Glu	Leu	Glu	Lys	Glu	Phe
ftz	Ser	Lys	Arg	Thr	Arg	Gln	Thr	Tyr	Thr	Arg	Tyr	Gln	Thr	Leu	Glu	Leu	Glu	Lys	Glu	Phe
Ubx	Arg	Arg	Arg	Gly	Arg	Gln	Thr	Tyr	Thr	Arg	Tyr	Gln	Thr	Leu	Glu	Leu	Glu	Lys	Glu	Phe

	21																			40
Hox-1	His	Phe	Asn	Arg	Tyr	Leu	Met	Arg	Pro	Arg	Arg	Val	Glu	Met	Ala	Asn	Leu	Leu	Asn	Leu
MM3	His	Phe	Asn	Arg	Tyr	Leu	Thr	Arg	Arg	Arg	Arg	Ile	Glu	Ile	Ala	His	Val	Leu	Cys	Leu
Antp	His	Phe	Asn	Arg	Tyr	Leu	Thr	Arg	Arg	Arg	Arg	Ile	Glu	Ile	Ala	His	Ala	Leu	Cys	Leu
ftz	His	Phe	Asn	Arg	Tyr	Ile	Thr	Arg	Arg	Arg	Arg	Ile	Asp	Ile	Ala	Asn	Ala	Leu	Ser	Leu
Ubx	His	Thr	Asn	His	Tyr	Leu	Thr	Arg	Arg	Arg	Arg	Ile	Glu	Met	Ala	Tyr	Ala	Leu	Cys	Leu

	41																			60
Hox-1	Thr	Glu	Arg	Gln	Ile	Lys	Ile	Trp	Phe	Gln	Asn	Arg	Arg	Met	Lys	Tyr	Lys	Lys	Asp	Gln
MM3	Thr	Glu	Arg	Gln	Ile	Lys	Ile	Trp	Phe	Gln	Asn	Arg	Arg	Met	Lys	Trp	Lys	Lys	Glu	Asn
Antp	Thr	Glu	Arg	Gln	Ile	Lys	Ile	Trp	Phe	Gln	Asn	Arg	Arg	Met	Lys	Trp	Lys	Lys	Glu	Asn
ftz	Ser	Glu	Arg	Gln	Ile	Lys	Ile	Trp	Phe	Gln	Asn	Arg	Arg	Met	Lys	Ser	Lys	Lys	Asp	Arg
Ubx	Thr	Glu	Arg	Gln	Ile	Lys	Ile	Trp	Phe	Gln	Asn	Arg	Arg	Met	Lys	Leu	Lys	Lys	Glu	Ile