with *Hoxb-4* associated with the most anterior cervical vertebra and *Hoxa-4* and *Hoxc-4* toward the middle of the cervical series, regardless of the specific number of neck vertebrae. The anterior expression boundary of *Hoxc-5* (the only *Hox-5* paralogue studied) marks the second-to-last cervical vertebra, which is number 13 in the chick and 6 in the mouse. *Hoxc-6* has an anterior boundary of expression at the level of the first thoracic vertebra (T-1) in all four animals; This is the eighth presacral vertebra in the mouse, the fifteenth in the chick, the eighteenth in the long-necked goose, and close behind the skull in the short-necked frog.

All of the paralogous genes of groups 7 and 8 have their anterior boundary of expression within the thoracic series. That of *Hoxa-9, Hoxb-9,* and *Hoxc-9* lies near the posterior end of the thoracic series, but the *Hoxd-9* boundary is near the lumbosacral transition, at somite level 29–30 in both chick and mouse. *Hox* genes *Hoxc-10* and *Hoxd-10* are expressed in the sacral region of the chick, but only the latter in the mouse. *Hoxd-11–Hoxd-13* are expressed in the tail of both species.

Burke et al. (1995) pointed out that the domains of *Hox* gene expression shift according to the functional anatomy of the vertebral regions in different vertebrate groups, rather than being tied to vertebral or somite number, suggesting that *Hox* genes may have played an important role in the evolution of axial variation. These changes might be explained either by different deployment of the upstream regulators of *Hox* expression, or through modification in the response to these regulators by the *Hox* genes themselves. The fact that individual members of paralogous groups have different sites of expression (e.g., the expression of *Hoxd-9* is more posterior than that of *Hoxa–c-9*) demonstrates that response to the same upstream regulators can differ, and suggests that the evolution of regulatory diversity within paralogous groups may have enabled major changes in morphology to occur without change in the basic function of the *Hox* genes.

The work by Burke and her colleagues shows the relationship between the position of *Hox* gene expression and regions of vertebral specialization, but does not show how their expression may influence the configuration of the vertebrae. This was investigated by Kostic and Capecchi (1994), based on gene disruption in the mouse. The most anterior limit of expression of *Hoxa-4* is at the level of the second cervical vertebra (C-2), the axis. This vertebra is characterized by a very large neural spine and an anterior extension of the centrum, the dens, that fits into the atlas. In all the mice that were homozygous for the disruption of *Hoxa-4,* the third cervical vertebra (C-3), which normally lacks a neural spine, develops one comparable to that normally expressed in the atlas; however, none of the other structures of C-3 is altered. Disruption of *Hoxb-4,* on the other hand, results in C-3 having a wide neural arch, like that of C-2, while C-2 develops a ventral tubercle that is normally expressed only in C-1, the atlas.

Kostic and Capecchi offered several alternatives to explain the different effects of disruption of *Hoxa* and *Hoxb*: action at different times during development (*Hoxb-4* before the neural arches have fused and *Hoxa-4* after fusion), regulation of different cell populations, or cell proliferation along different planes.

While disruption of the genes usually expressed in the second and third cervical vertebrae resulted in their characteristics being transformed anteriorly, disruption of *Hoxa-6,* which is usually expressed in the last cervical, resulted in its characteristics being transformed posteriorly. In normal mice, the configuration of the axial skeleton changes conspicuously between the last cervical (C-7) and the first thorac-