Homeotic Gene Expression in Vertebrates

A fundamental question in developmental biology concerns how a cell knows where it is, relative to other cells and to the overall body plan. Position signalling (as it is called) is very important during early embryologic development and also in linearly ordered processes such as skeletal growth. Much is known about position signalling in lower species, such as *Drosophila*, in which so-called homeotic selection genes appear to serve as master genes controlling expression of many other genes in the developing embryo. These master genes contain highly conserved (homeobox) sequences that code for DNA binding protein domains and are organized as clusters of contiguous genes on chromosomes. Their expression is segmentally distributed, providing information about the anterior-posterior position of cells within an embryo. Interestingly, there is a spatial relationship between the chromosomal order of the genes and the location of their expression in the embryo, such that the genes within a homeobox are sequentially expressed congruently with their anterior to posterior expression in the body.

Homeotic genes and gene clusters have been identified in higher species, including humans, but their functional similarity has been questioned because genesis of vertebrate and insect bodies differs so much. In particular, segmentation, which demarcates the limits of expression of the insect homeotic genes, has been thought to occur in a different fashion in vertebrates. However, a report by Wilkinson et al suggests that segmental expression of homeotic genes does occur in vertebrate embryos. Using in situ hybridization, these investigators demonstrated that expression of four contiguous murine homeotic genes (Hox 2.1, 2.6, 2.7, 2.8) exhibited a segmental distribution in the hindbrain of 9.5-day-old mouse embryos. The anterior limits of expression jumped by two segment intervals and the order of segmental expression corresponded to the chromosomal order of the gene loci. Hence, as with *Drosophila,* there is a physical relationship between the chromosomal order of gene loci and their segmental expression along the anterior-posterior axis of the early embryo.

Wilkinson DG, Bhatt S, Cook M, et al. *Nature* 1989;341:404-409.

Editor's comment—*The segmental expression of homeotic genes in the mouse hindbrain seems far removed from growth in humans. However, as one strives to understand human growth and development at the cellular and molecular levels, one becomes more dependent on knowledge acquired from lower organisms. Finding similarities between man and distant species in fundamental processes, such as positional signalling, greatly facilitates this task.*

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