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Preface

Hox and ParaHox Genes in Evolution, Development and Genomics

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The discovery of the homeobox motif and its presence in each gene of the Hox clusters revolutionized the fields of developmental biology and evolutionary developmental biology (*1, 2*), providing a rapid entrance into investigating the mechanisms of development of almost any animal taxon as well as dramatically altering conceptions on the extent of genetic conservation across the animal kingdom. The wide-reaching implications stemming from Hox biology and the rapid developments in the field due to technological advances, such as improved sequencing techniques and RNAi, make this special issue of *Genomics, Proteomics & Bioinformatics* a timely marker of progress.

Despite the intensive research on Hox genes over the last few decades, much about the biology of these genes remains mysterious. Focusing investigations on powerful genetic model species, such as fruit flies and mice, have contributed much to our understanding. However, the comparative approach, involving studying the genes in non-traditional model systems that are primarily selected for their position within the animal phylogeny rather than their immediate tractability in the lab, has been vital to the progress of Hox biology, even from its earliest days. A prime example of this was the discovery that the ParaHox genes probably evolved as an evolutionary sister cluster to the Hox cluster, deep in animal ancestry (*3*). Consequently, the review articles in this special issue are written with this comparative emphasis to the fore.

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Hox and ParaHox genes are thought to pattern the anterior–posterior development of nearly all animals, with the homeobox motif encoding a DNA-binding domain (the homeodomain) that is 60 amino acids long and makes sequence-specific contacts with the regulatory regions of target genes. These Hox/ParaHox genes thus encode transcription factors that direct major developmental pathways and gene networks. The homeobox family of genes is, however, large and much more extensive than Hox and ParaHox genes alone. All Hox genes are homeobox genes, but not all homeobox genes are Hox genes. The term "Hox" is now restricted, when used properly, to naming genes that are orthologous to the genes in the mouse Hox gene clusters (*4, 5*). The organization of the Hox and ParaHox genes in ordered clusters in the genome, with the order of the genes along the chromosome being colinear with the position (and often time) at which they are expressed during embryogenesis, has been one of the leitmotifs of Hox/ParaHox biology, but remains poorly understood. This ordered cluster organization is certainly linked to the function of these genes in some lineages (*5*), but is subject to much change during animal evolution, with potentially significant evolutionary and developmental implications, as outlined in the accompanying reviews.

The review articles assembled here can be viewed as having a phylogenetically nested format. Firstly, Moreno *et al* (*6*) provide an overview of Hox/ParaHox gene function and organization in the acoel flatworms, a phylum likely occupying a key position as a basal bilaterian lineage (*7*) [or possibly even as an early branching lineage within the deu-

terostomes themselves (*8*)]. Next, Ikuta (*9*) takes us into the realm of the traditionally recognized invertebrate deuterostomes: the invertebrate chordates, hemichordates and echinoderms. Finally, the latest understanding of the evolution of vertebrate Hox cluster organization is described by Kuraku (*10*). Throughout these reviews, there is a common theme of the important links between the evolution of genome organization and the role of these genes in the evolution of development, with the need to study a wide range of animal lineages in order to truly understand the fundamentals of Hox/ParaHox biology being evident.

References

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