

Hox Genes and the Evolution of Vertebrate Axial Morphology Experiment (1995) [1]

By: Brinkman, Joe Keywords: [Hox](#) [2] [Hox Genes](#) [3]

In 1995, researchers Ann Burke, Craig Nelson, Bruce Morgan, and Cliff Tabin in the US studied the [genes](#) [5] that regulate the construction of vertebra in developing [chick](#) [6] and [mouse](#) [7] embryos, they showed similar patterns of gene [regulation](#) [8] across both species, and they concluded that those patterns were inherited from an ancestor common to all vertebrate animals. The group analyzed the head-to-tail (anterior-posterior) axial development of vertebrates, as the [anterior-posterior axis](#) [9] showed variation between species over the course of evolutionary time. Along those axes, they showed where [Hox genes](#) [5] produced RNAs. [Hox genes](#) [5] have the [homeobox](#) [10], a portion of DNA contributes to the generation of the body plans of animals, plants, and fungi. In the 1995 study, the researchers compared the expression patterns of [Hox genes](#) [5] across the [chick](#) [6] and [mouse](#) [7] embryos, showing where the patterns were similar and where they differed. Based on those comparisons, they argued that [Hox genes](#) [5] were present in the ancestors of tetrapods and fishes, and that [Hox genes](#) [5] function in the [segmentation](#) [11] of the anterior-posterior vertebrate axis in both [chick](#) [6] and [mouse](#) [7] embryos.

A team led by [Walter Jakob Gehring](#) [12] observed the [homeobox](#) [10] in a 1984 study at the [University of Basel](#) [13] in Basel, Switzerland. While isolating the *Antennapedia* gene in [Drosophila](#) [14], Gehring noticed genetic sequences that were common (homologies) between the *Antennapedia* gene and a neighboring gene that controlled [segmentation](#) [11] in the embryo. Scientists named the segment of homology between those [genes](#) [5] the [homeobox](#) [10], and scientists later showed that the [homeobox](#) [10] encoded for [Hox genes](#) [5] that help specify body plans. Accumulating research showed that the [homeobox](#) [10] exists among both vertebrates and invertebrates, and that it typically functions in anterior-posterior development. In 1990, Michael Kessel and colleagues proposed that [Hox genes](#) [5] determine the [morphology](#) [15] of individual vertebrae in mice. Due to the 1990 studies, Bruce, Burke, Nelson, and Tabin conducted further experiments in [mouse](#) [7] and [chick](#) [6] embryos to better understand the evolutionary homology and comparable development of [Hox genes](#) [5] in the organisms that contain them.

Ann Burke, at [Wesleyan University](#) [16] in Middletown, Connecticut, studied the [evolution](#) [17] of body structure in vertebrates. Craig Nelson, at the University of Connecticut in Storrs, Connecticut, also studied how vertebrate animals evolved. These two scientists collaborated with Bruce Morgan and Cliff Tabin, at [Harvard Medical School](#) [18] in Boston, Massachusetts. The focus of Tabin's research was on how [genes](#) [5] help produce structures in developing vertebrate animals, while Morgan focused on how [genes](#) [5] formed appendages in vertebrates. The group came together in 1995 to investigate to study how different developmental processes evolved. The group studied chicks ([gallus gallus](#) [19]) and [mouse](#) [7] ([mus musculus](#) [20]) embryos. They studied twenty-three [Hox genes](#) [5] in chicks and sixteen [Hox genes](#) [5] in mice, all of which they grouped into thirteen paralogue groups, or groups that are genetically related after duplication occurs within the [genome](#) [21]. The researchers analyzed the expression of those groups in mice and in chicks to analyze the similarities and differences of [Hox](#) gene expression across species.

The group analyzed the boundaries of [Hox](#) gene expression of [chick](#) [6] and [mouse](#) [7] embryos by means of *in situ* hybridization. *In situ* hybridization is a technique that uses complementary DNA (cDNA) templates, or double stranded DNA synthesized from messenger RNA templates, to locate a specific nucleic acid sequence, and it helps the sequence of interest to become visible. Bruce, Burke, Nelson, and Tabin used *in situ* hybridization to find the relationship between [Hox](#) gene expression, or the amount of RNA produced by each [Hox](#) gene, and morphological boundaries along the anterior-posterior body axis in [chick](#) [6] and [mouse](#) [7] embryos. Specifically, the four scientists focused on sixteen [Hox genes](#) [5] that they thought functioned in axial development, or development of the central part of the body in chicks and mice. There were four kinds of [Hox](#) gene clusters, called *Hoxa*, *Hoxb*, *Hoxc*, and *Hoxd*.

Paralogue group four showed expression, or produced RNAs, within the cervical (neck) region of both the [chick](#) [6] and [mouse](#) [7]. Specifically, *Hoxa-4*, *Hoxb-4* *Hoxc-4* [genes](#) [5] expressed within the cervical region in the organisms. *Hoxa-4* expressed in the anterior cervical vertebrae, and *Hoxb-4* and *Hoxc-4* express toward the middle cervical vertebrae. The researchers observed *Hoxb-8*, *Hoxc-8*, *Hoxd-8* [genes](#) [5], all three members of the eighth paralogue group, in both the [chick](#) [6] and [mouse](#) [7] embryos. In both [mouse](#) [7] and [chick](#) [6] embryos, the *Hoxc-8* [genes](#) [5] functioned in the cells bordering vertebra, the fifth thoracic vertebrae in the [chick](#) [6], and the sixth thoracic vertebrae in mice. *Hoxd-8* and *Hoxb-8* resulted in an unclear anterior-posterior area of gene expression in both species. The entire ninth paralogue expressed close to the end of the thoracic vertebrae in both animals,

showing gene expression for four segments behind the forelimb in the [chick](#)^[6] and nine segments behind the forelimb in the [mouse](#)^[7]. All *Hox10* paralogues expressed close to the lower spine (lumbosacral) region in both organisms, with *Hoxd-10* expressed at the first sacral vertebra in both the [chick](#)^[6] and [mouse](#)^[7] embryos. Parologue groups eleven through thirteen did not show gene expression as close together as the other groups, although groups eleven through thirteen all showed gene expression in the sacral and tail region of the embryos.

In their research report, the researchers hypothesized from their results that *Hox genes*^[5] played a role in vertebrate [evolution](#)^[17]. The researchers noted that the *Hox* gene expression of [genes](#)^[5] in parologue groups four through thirteen showed remarkably similar morphological expression among the [chick](#)^[6] and [mouse](#)^[7] embryos. They also noted that despite the significantly different overall body structure between the two organisms, specific anatomical areas, such as the vertebrae, showed a correlation in the types of individual [genes](#)^[5] that were expressed. The researchers suggested that the correlation demonstrates that *Hox genes*^[5] function in the [segmentation](#)^[11] of the anterior-posterior vertebrate axis in both organisms. The researchers proposed that the minor shifts in developmental spacing of the [genes](#)^[5], as noted with parologue group nine, are caused by expansion or shortening of a specific body region, and not from differential expression of the [genes](#)^[5] themselves. From those observations, the researchers argued that *Hox genes*^[5] play a crucial role in the [evolution](#)^[17] of axial variation and thus the [evolution](#)^[17] of tetrapods.

The researchers hypothesized that the full range of *Hox genes*^[5] were present in the common ancestor of tetrapods and fishes. Although lacking the axial regions seen in tetrapods, they claimed that it is almost certain that the *Hox genes*^[5] played a role of anterior-posterior definition in this common ancestor. The research report became highly cited, prompting hundreds of similar studies, and propelling the burgeoning field of [evolutionary developmental biology](#)^[22].

Sources

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