

Ed Lewis, c. 1950

*bx, pbx/Ubx*

Genetic map of Bithorax complex

Diagram showing the genetic map of the Bithorax complex with genes: *abx*, *bx*, *Cbx*, *Ubx*, *bx-d*, *pbx*, *Hab*, *lab-2*, *lab-3*, *Ubx*, *Mcp*, *lab-5*, *lab-6*. Below the map is a schematic of the protein structure with domains labeled C, D, and E.

Cloning of Bx-C and molecular map ~1983

Diagram showing the molecular map of the Bx-C complex with genes: *abx / pbx*, *bx-d / pbx*, *lab-2*, *lab-3*, *lab-4*, *lab-5*, *lab-6*, *lab-7*, *lab-8*. The map includes a scale from -100 to +200 and labels for *Ubx*, *abdA*, and *AbdB*.

Discovery of homeobox, 1984

Homeodomain bound to DNA

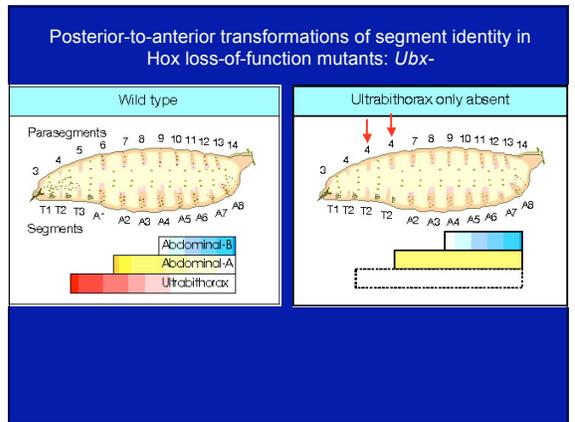
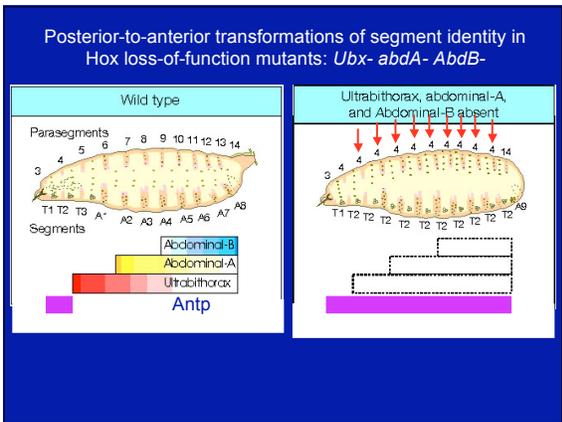
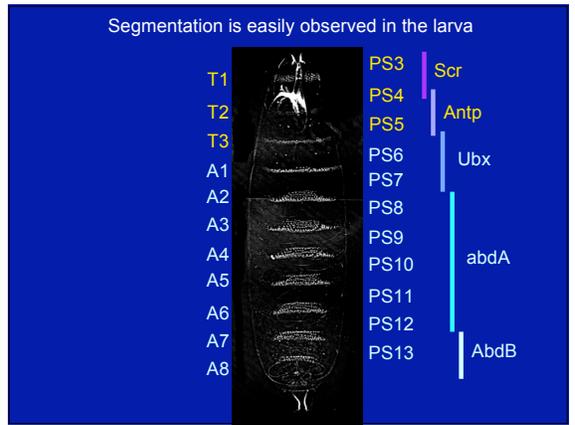
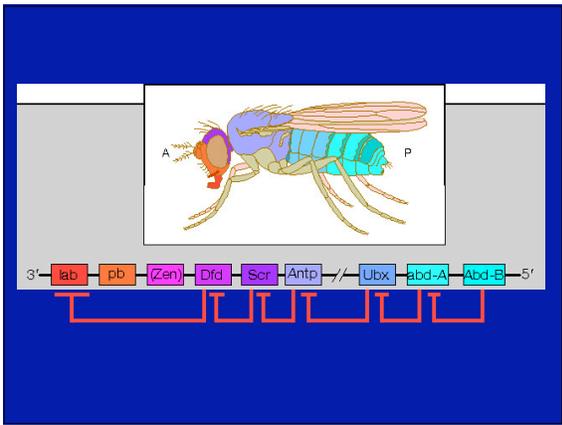
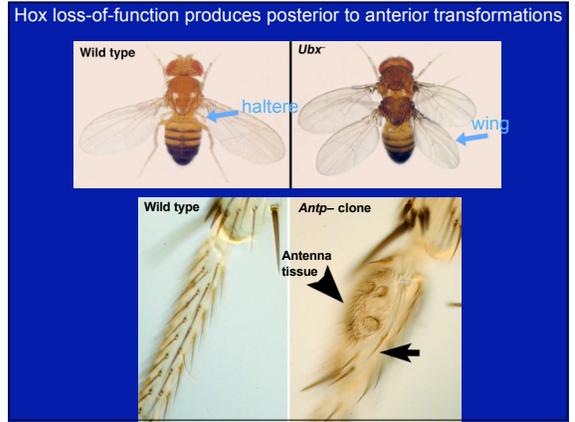
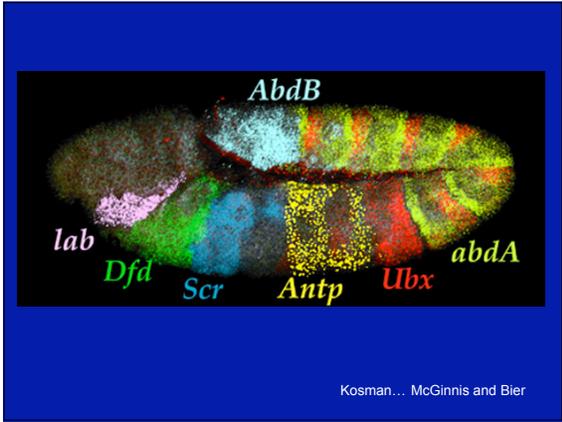
Hox proteins are homeodomain-containing transcription factors

Diagram showing the structure of a homeodomain protein with N and C termini. It highlights highly conserved regions, a YPWM motif, and a homeodomain. A 3D model below shows helix 1, helix 2, helix 3, a turn, and the N-terminal arm.

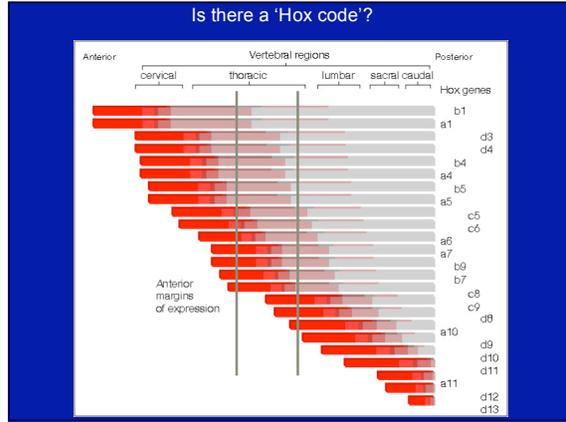
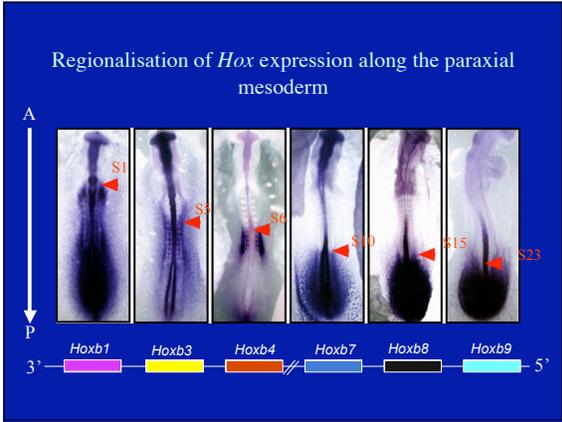
Homeodomains are everywhere

Phylogenetic tree showing the distribution of homeodomain proteins across various species, with a bracket indicating the Hox cluster.

Diagram showing the Antennapedia complex (*lab*, *pb*, *Zen*, *Dfd*, *Scr*, *Antp*) and the Bithorax complex (*Ubx*, *abd-A*, *Abd-B*) in a fly. The fly is labeled with 'A' for Antennapedia and 'P' for Bithorax.



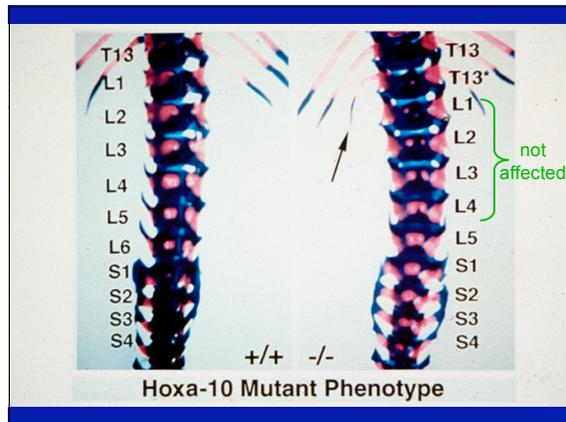
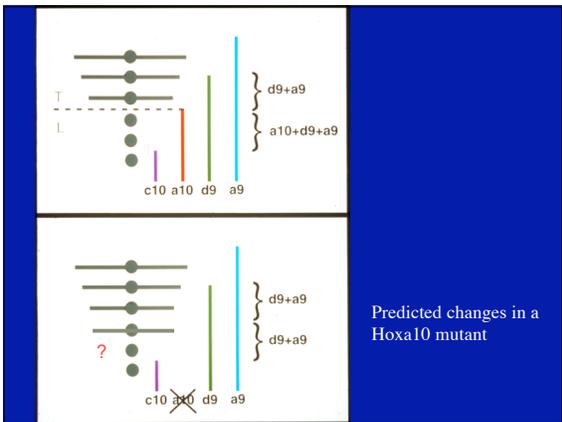
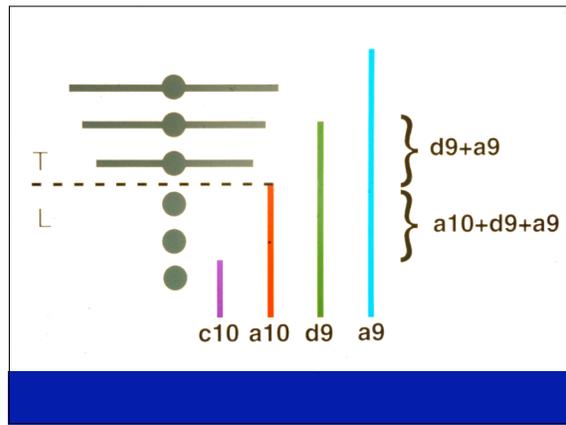




### Different *Hox* genes correlate with different vertebral morphologies

HOX CODE ASSIGNMENT TO VERTEBRAL COLUMN

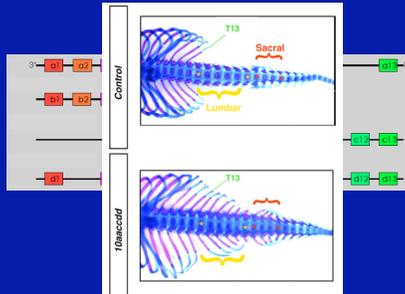
Gene	Axis	Axis	C-3	C-4	C-5	C-6	C-7	T-1	T-2
Hox-1.6	+	+	+	+	+	+	+	+	+
Hox-1.5	+	+	+	+	+	+	+	+	+
Hox-2.6	+	+	+	+	+	+	+	+	+
Hox-4.2	+	+	+	+	+	+	+	+	+
Hox-1.4	+	+	+	+	+	+	+	+	+
Hox-2.1			+	+	+	+	+	+	+
Hox-1.3			+	+	+	+	+	+	+
Hox-2.5					+	+	+	+	+
Hox-3.4						+	+	+	+
Hox-3.3							+	+	+
Hox-1.2								+	+



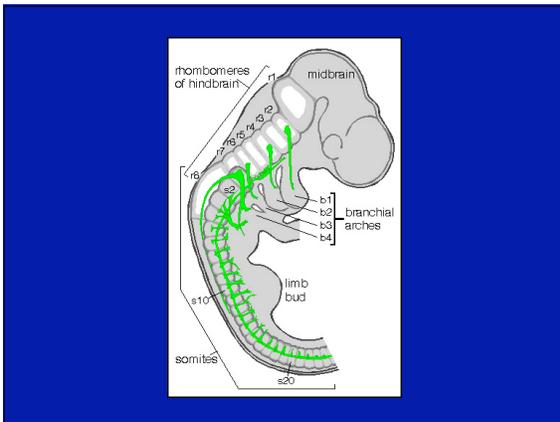
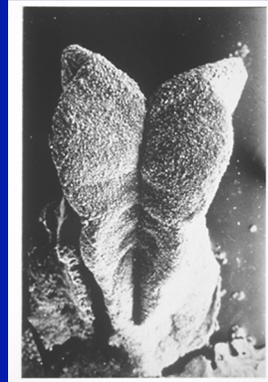
This analysis has been complicated by genetic redundancy—the expression and function of two or more similar *Hox* genes in overlapping domains.

Paralogs are expressed in similar domains, and substitute for each other.

When all *Hox10* paralogs are mutated, no lumbar vertebrae form, and instead, ribs project from all posterior vertebrae.

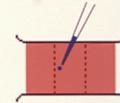


### Transient segmentation of the hindbrain

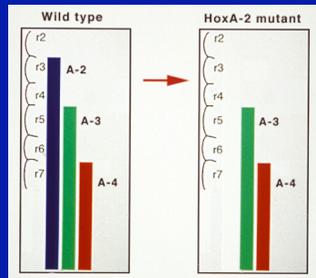
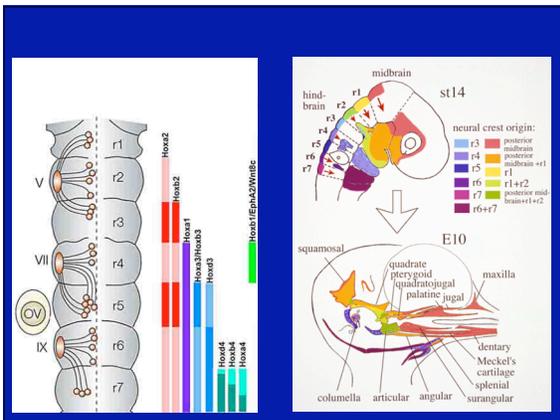


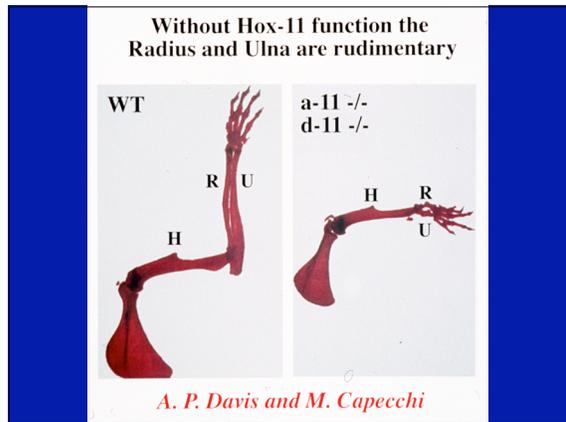
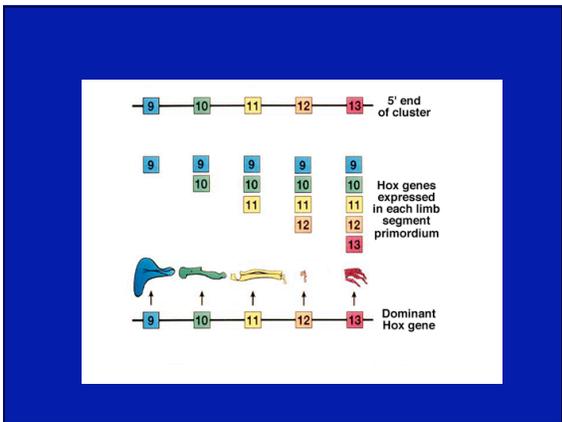
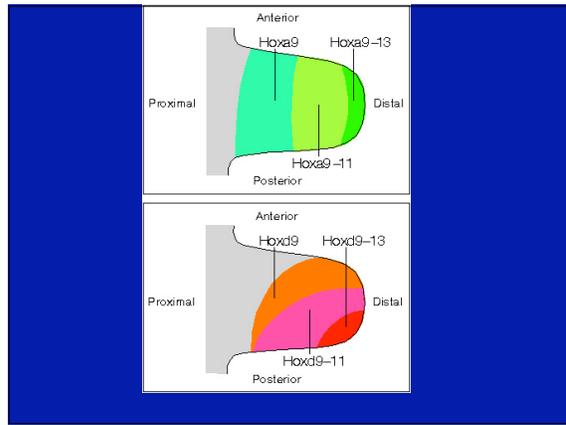
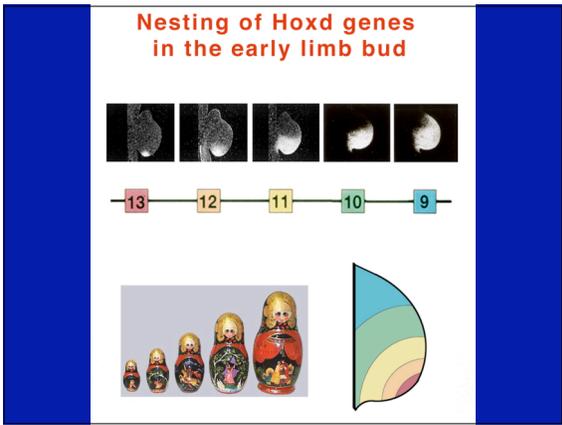
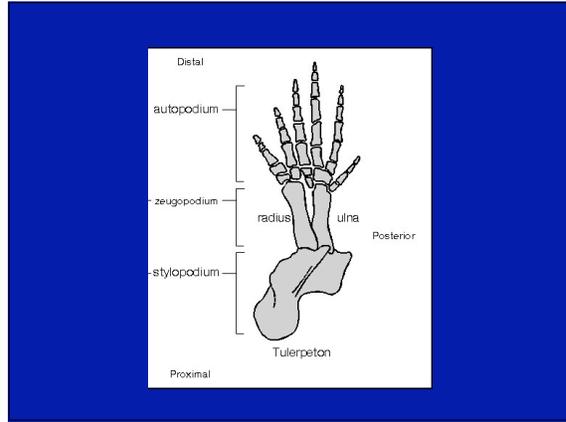
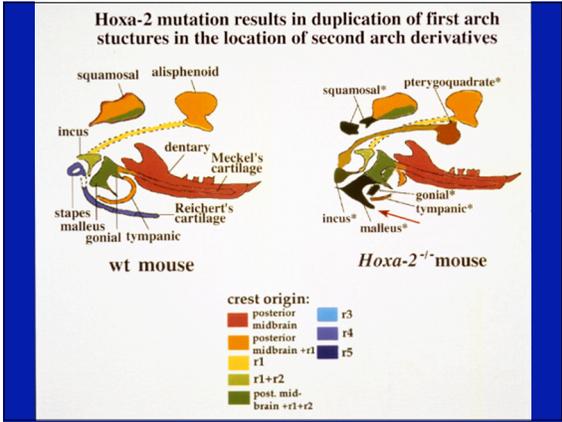
Rhombomeres are developmental "compartments" ie cell populations with distinct fates, which do not mix

Mark a cell prior to morphological formation of teh Rhombomeres



Resultant clone does not cross Rhombomere boundaries

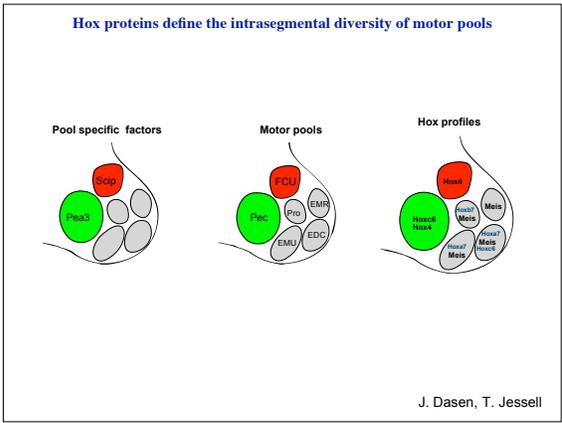
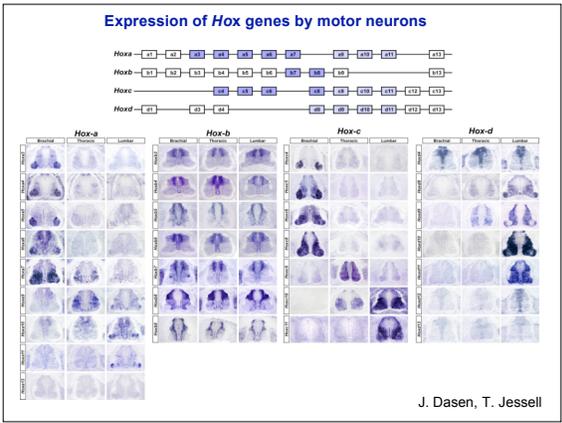
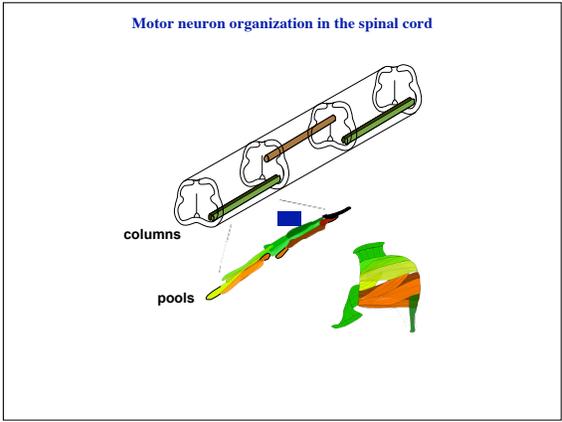




Synpolydactyly can be caused by alanine repeat expansions in Hox D13

A: Normal hand  
B: Hand with synpolydactyly (extra digits)  
C: Feet with synpolydactyly

Hox gene clusters: 9, 10, 11, 12, 13 (Dominant Hox gene)

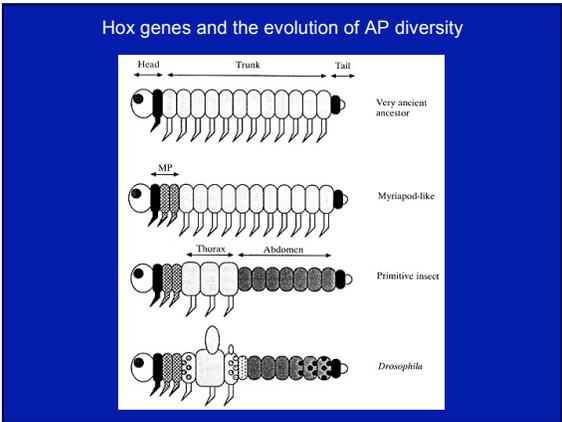


What can evolutionary comparisons tell about Hox function?

Drosophila: Hox, Antp, Ubx, AbdA, AbdB, AbdC, AbdD, AbdE, AbdF, AbdG, AbdH, AbdI, AbdJ, AbdK, AbdL, AbdM, AbdN, AbdO, AbdP, AbdQ, AbdR, AbdS, AbdT, AbdU, AbdV, AbdW, AbdX, AbdY, AbdZ, AbdA', AbdB', AbdC', AbdD', AbdE', AbdF', AbdG', AbdH', AbdI', AbdJ', AbdK', AbdL', AbdM', AbdN', AbdO', AbdP', AbdQ', AbdR', AbdS', AbdT', AbdU', AbdV', AbdW', AbdX', AbdY', AbdZ'

Mouse: Hoxa, Hoxb, Hoxc, Hoxd clusters on chromosomes 6, 11, 15, and 2.

A: Anterior, P: Posterior



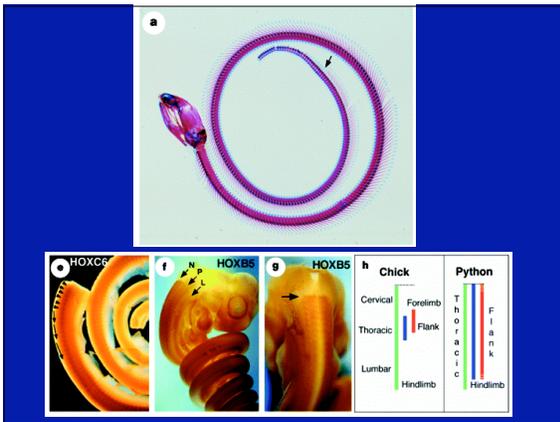
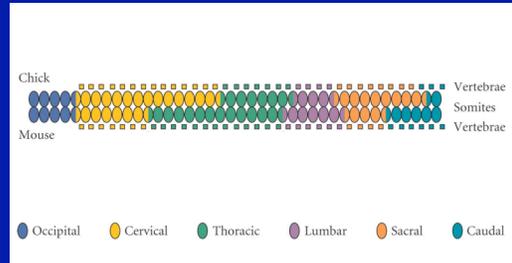
Human Hox genes work in the fly to make fly structures

Wild type fly antenna      Antenna to leg transformation induced by HoxB6

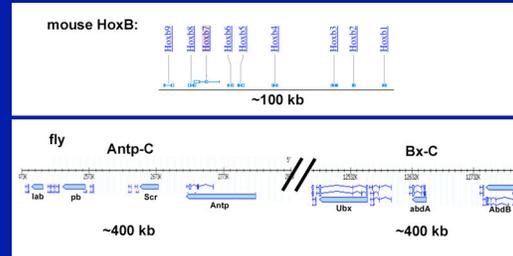


W. McGinnis, L. Pick

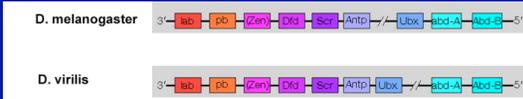
Mouse and Chick Vertebral Pattern along the Anterior-Posterior Axis



Differences between fly Hox and vertebrate Hox

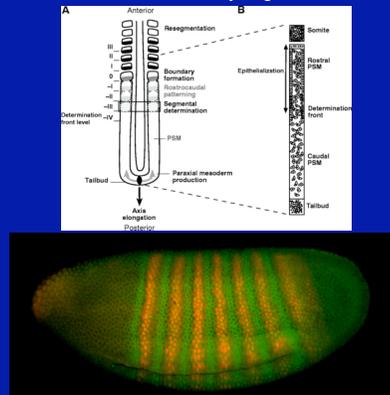


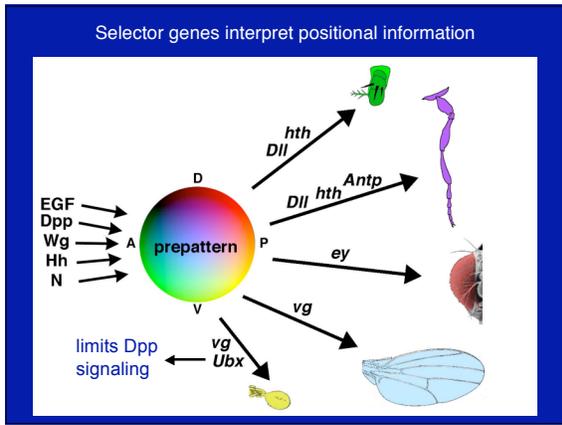
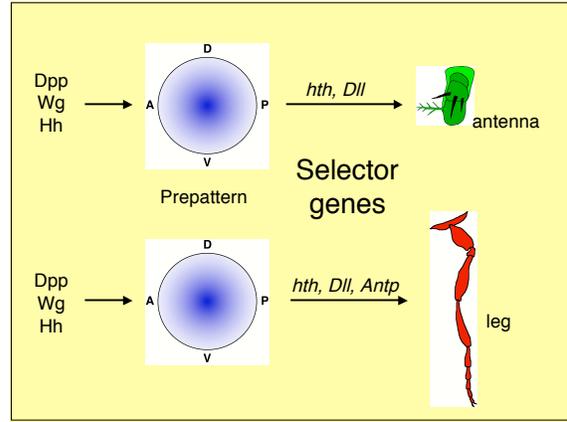
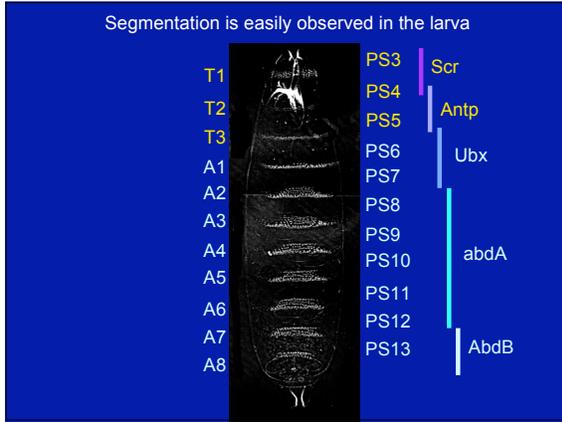
Differences between fly Hox and fly Hox



Conclusion: although still in clusters, the invertebrate complexes are 'falling apart', whereas the vertebrate clusters have retained their integrity, probably because of the way their expression is regulated.

Big differences in vertebrate and fly segmentation mechanisms





Literature:

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