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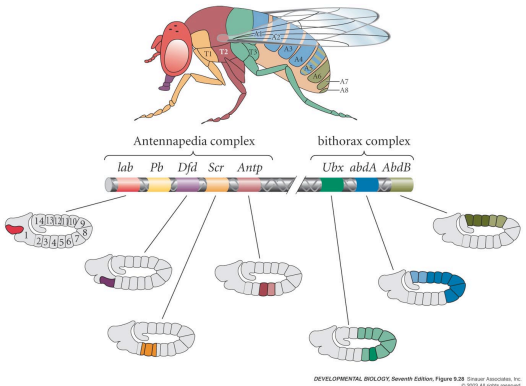
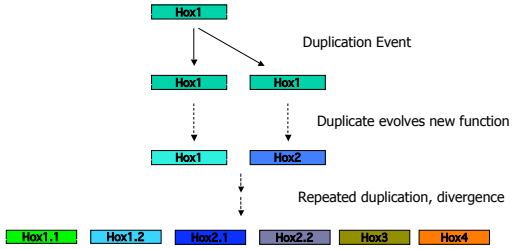
The Rosetta Stone - discovered in 1799 by the French under Napoleon, surrendered to the British. Now resides in London in the British Museum.

Contains a proclamation in Greek and Egyptian (hieroglyphics and demotic) from the Ptolemeic era (196 BC).

Figure 9.28 ***Homeotic Gene Expression in*** **Drosophila**

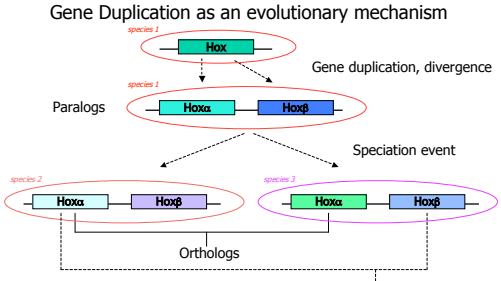


Gene Duplication as an evolutionary mechanism



A homeotic gene complex (HOM-C) was present in the ancestor of all animals, patterning the anterior-posterior axis.

Gene Duplication as an evolutionary mechanism



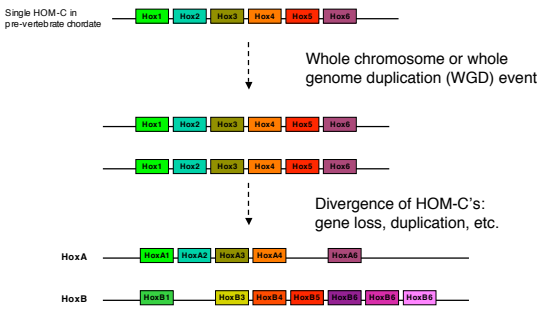
Gene evolutionary relationships

Homologs - share a common ancestor

Paralogs - arise by gene duplication event

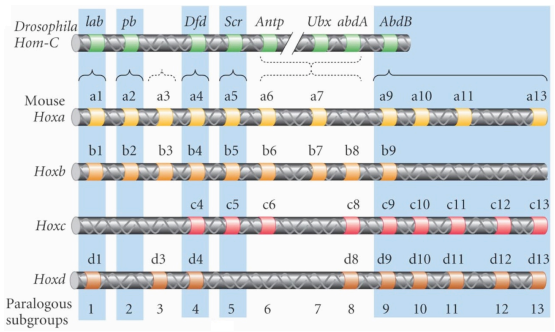
Orthologs - arise by speciation event

HOM-C Complex Duplication occurred in vertebrate evolution



Most vertebrates have four HOM-C's; teleost fish have up to seven

Figure 11.42(1) ***Evolutionary Conservation of Homeotic Gene Organization and Transcriptional Expression***



Orthologs: e.g., *lab* & *Hoxa1, Dfd & Hoxc4*

Evolutionary Conservation of Homeodomain Amino Acid Sequences

```
                                  Antp group
Fruit fly      RKRGRQTYTRYQTLELEKEFHFNRYLTRRRRIEIAHALCLTERQIKIWFQNRRMKWKKEN
Centipede      RKRGRQTYTRYQTLELEKEFHFNRYLTRRRRIEIAHALCLTERQIKIWFQNRRMKWKKEN
Spider         RKRGRQTYTRYQTLELEKEFHFNRYLTRRRRIEIAHALCLTERQIKIWFQNRRMKWKKEN
Leech          QKRTRQTYTRYQTLELEKEFYSNRYLTRRRRIEIAHSLALSERQIKIWFQNRRMKWKKEN
Sea urchin     GKRGRQTYTRQQTLELEKEFHFSRYVTRRRRFEIAQSLGLSERQIKIWFQNRRMKWKREH
Zebra fish     GRRGRQTYTRYQTLELEKEFHFNRYLTRRRRIEIAHALCLTERQIKIWFQNRRMKWKKEN
Mouse          GRRGRQTYTRYQTLELEKEFHYNRYLTRRRRIEIAHALCLTERQIKIWFQNRRMKWKKES
Human          GRRGRQTYTRYQTLELEKEFHYNRYLTRRRRIEIAHALCLTERQIKIWFQNRRMKWKKES
```

Antp-class homeodomain protein HD regions from various animals

The HOM-C is a primordial A-P patterning system in animals

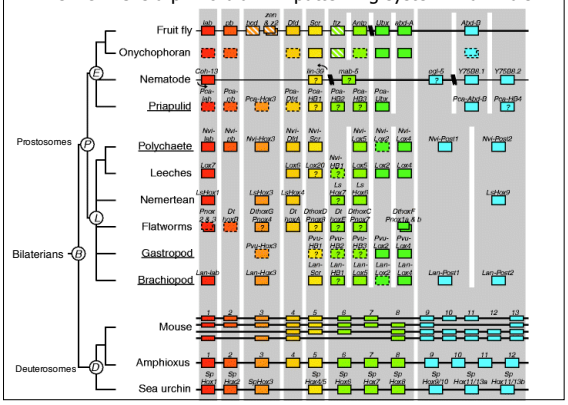
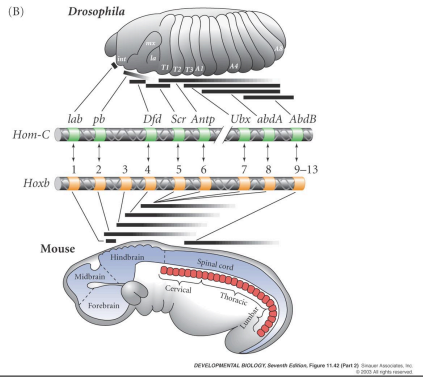


Figure 11.42(2) ***Evolutionary Conservation of Homeotic Gene Organization and Transcriptional Expression***



Mammalian HOM-C gene function

Mammalian HOM-C genes are found in clusters, and are expressed in A-P pattern related to location on chromosomes.

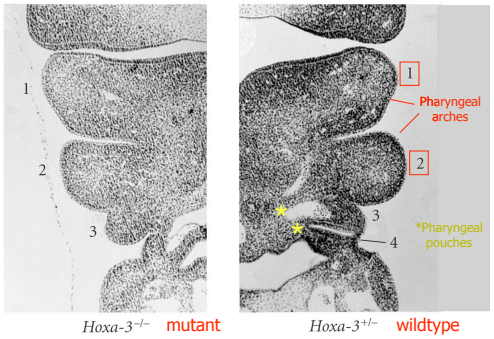
Do they function to specify regional identity, like in *Drosophila*?

Mouse "gene knockouts" used to address this question.
(2007 Nobel - work by Capecchi, Smithies & Evans)

Basic answer:
Yes - mouse Hox mutants have homeotic transformations.

(Examples follow)

Figure 11.43 ***Deficient Development of Neural Crest-Derived Pharyngeal Arch and Pouch Structures in* Hoxa-3-*Deficient Mice***



From Chisaka & Cappechi, 1991

Vertebral Transformations caused by Hox mutations

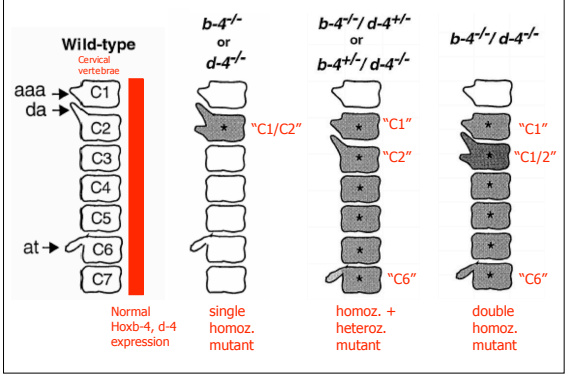
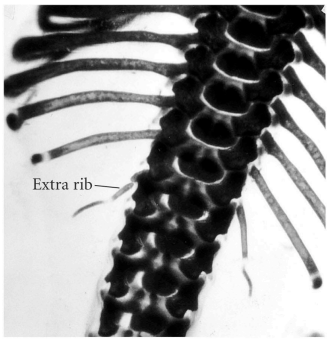
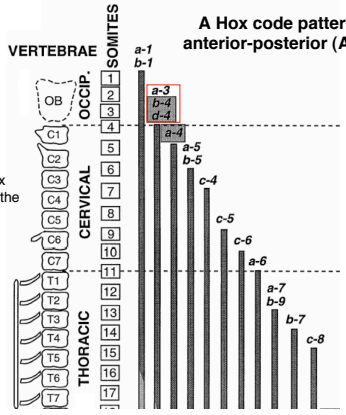


Figure 11.44 ***Partial Transformation of the First Lumbar Vertebra into a Thoracic Vertebra by the Knockout of the*** **Hoxc-8** ***Gene***

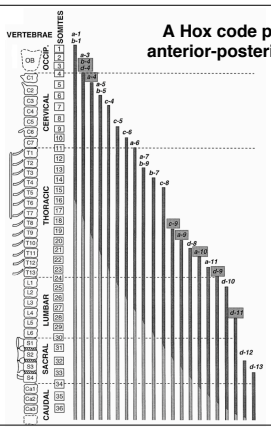


A Hox code patterns the anterior-posterior (A-P) axis

Mesodermal Hox code patterning the axial skeleton



Mesodermal Hox code patterning the axial skeleton



Hox genes activated in part by endogenous retinoic acid (RA)

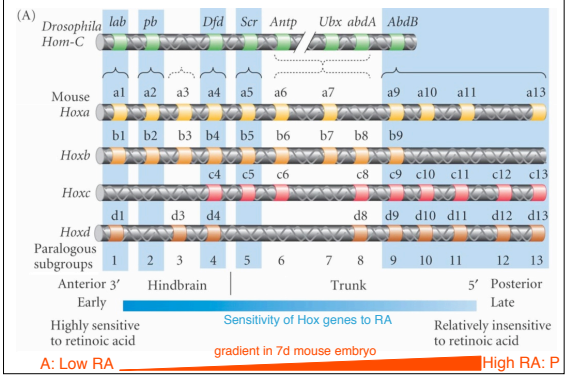
Many HOM-C genes have RA receptor-binding enhancers

Early embryo has A-P gradient of RA (lo - anterior, hi - posterior)

Hensen's node also has RA (varying conc. over time)

Hox genes vary in sensitivity to RA
(generally low sensitivity in posterior, high sensitivity in anterior)

Figure 11.42(1) ***Evolutionary Conservation of Homeotic Gene Organization and Transcriptional Expression***



Hox genes activated in part by endogenous retinoic acid (RA)

Exogenous RA is a powerful teratogen.

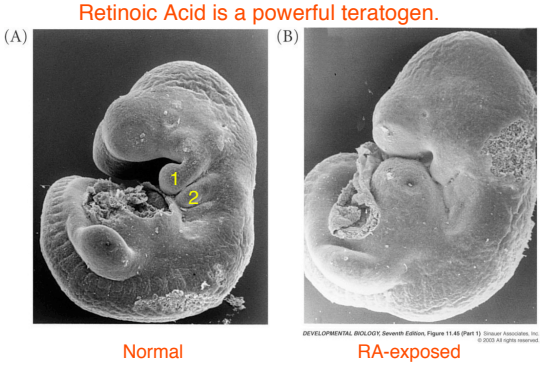
Exposure to additional RA typically causes structures to be transformed to more anterior

Transformations consistent with shifts in Hox gene expression - 'anterior' Hox genes expressed further posterior

Some exposure causes complete loss of many posterior structures

Figure 11.45(1) ***The Effect of Retinoic Acid on Mouse Embryos***

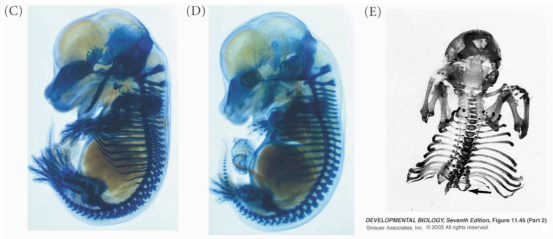
Retinoic Acid is a powerful teratogen.



Normal RA-exposed

Figure 11.45(2) ***The Effect of Retinoic Acid on Mouse Embryos***

High RA (exogenous) turns on "anterior" HOM-C genes



Normal RA-exposed RA-exposed: loss of most posterior structures

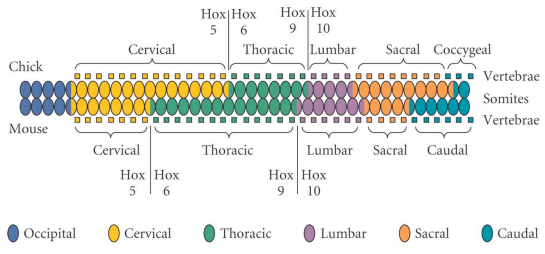
The Hox gene 'code' may explain evolutionary changes

Boundaries between Hox gene expression define body regions (seen clearly in axial skeleton).

Regions of Hox gene expression in mammals vs. birds are consistent with differences in numbers of vertebral types.

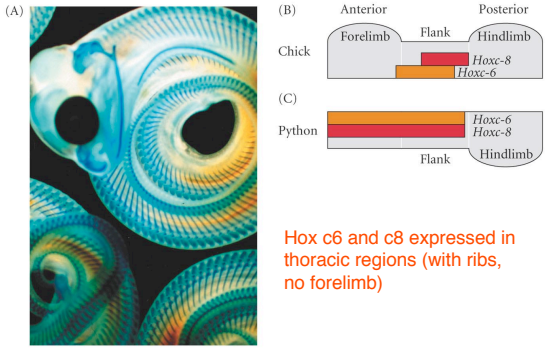
For example, the boundary between cervical and thoracic vertebrae is marked by the Hox group 5 and 6 boundary.

Figure 11.46 ***Mouse and Chick Vertebral Pattern along the Anterior-Posterior Axis***



Hox gene expression correlates with vertebral type

Figure 23.9 ***Loss of Limbs in Snakes***



Hox c6 and c8 expressed in thoracic regions (with ribs, no forelimb)

Figure 23.11 ***Postulated Ancestry of the Hox Genes From a Hypothetical Ancestor***