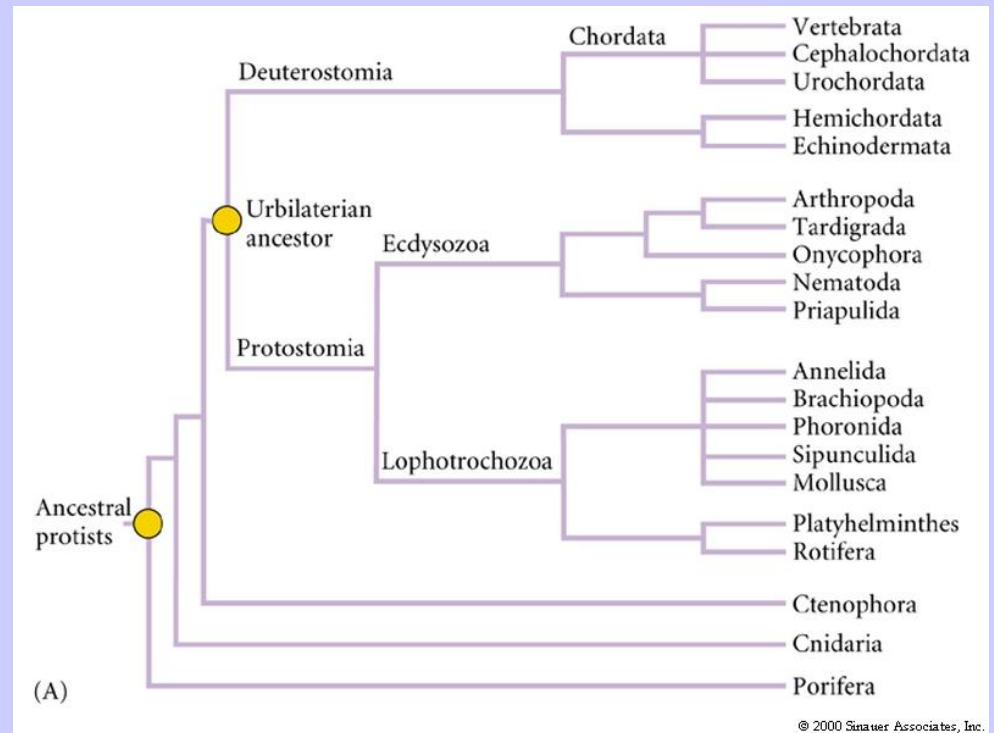


# Evo-Devo

Developmental Mechanisms of  
Evolutionary Change

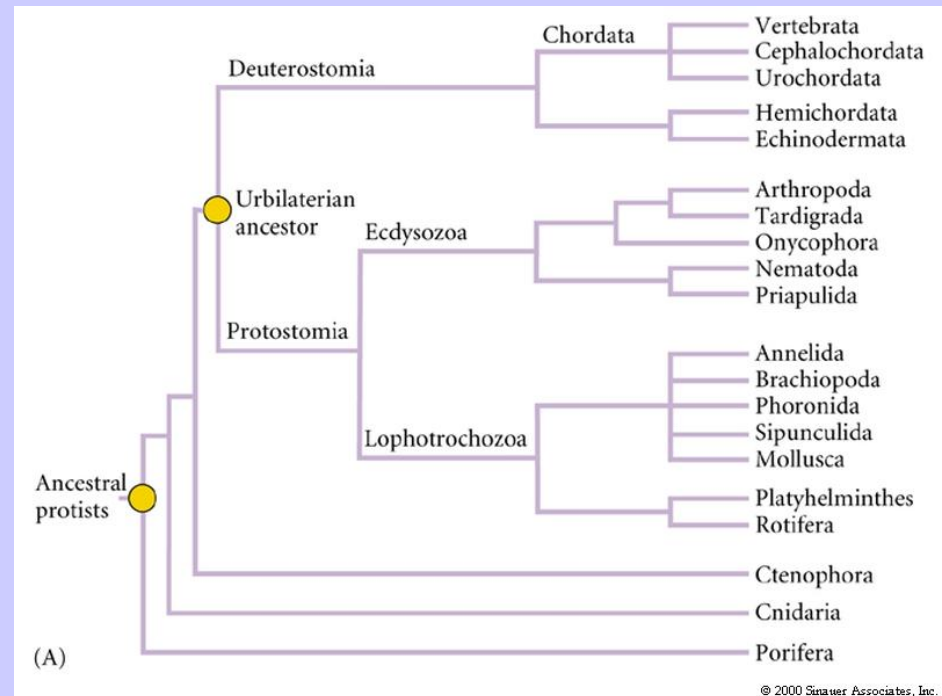
# Modern Phylogenetic Tree

- Lines of evidence
  - total DNA sequences
  - regulatory genes
  - new morphology
- Computer programs to analyze



# Modern Phylogenetic Tree

- Kingdoms
  - Porifera
  - Cniderians and Ctenophores
  - Bilateria
- 0, 2 and 3 tissue layers respectively



# Bilateria

- Deuterstomes
  - chordates (e.g. vertebrates)
  - echinoderms and hemichordates
- Protostomes
  - ecdysozoa
    - exoskeletons, molt (e.g. nematodes and arthropods)
  - lophotrochozoa
    - soft (e.g. molluscs, flatworms, segmented worms)

# What Have We Learned?

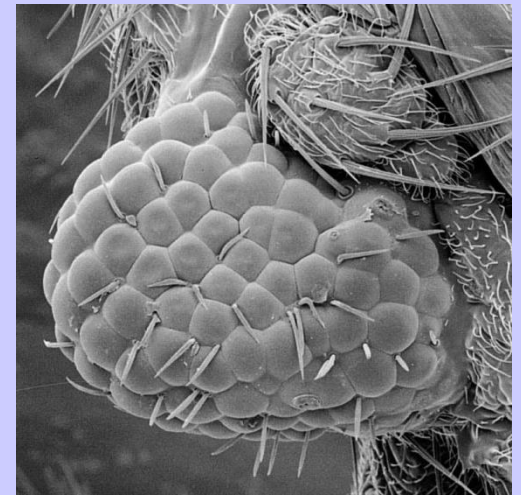
- Behind developmental change there are
  - transcription factors
    - differential gene expression patterns for differentiation
    - and gross changes in pattern
  - signaling pathways
    - integration of changes
      - physiological
      - morphological
      - transcriptional
    - intercellular and extracellular
    - = classical morphogens and inducers

# Historical Overview

- New insights from
  - developmental genetics (gene regulation)
  - cell biology of signaling pathways
- Idea
  - interacting networks
  - changes in a few things give major changes in pattern
  - in lab sometimes lethal
  - in nature?

# Common Regulatory Genes

- Urbilaterian ancestor should have had genes still found in deuterostomes and protostomes
  - *Pax6* in vertebrates and *eyeless* in fruit flies
    - eye formation
  - *Nkx 2-5* in mouse and *tinman* in fruit flies
    - heart formation
  - *Otx, Emx* in frogs and mice, *otd, emx* in fruit flies
    - anterior head and nerve structures



Mouse Pax 6 expressed in *Drosophila* leg

**TABLE 23.1** Developmental regulatory genes conserved between protostomes and deuterostomes (*Part 2*)

Gene	Function	Distribution
<i>Otx-1, Otx-2/Otd, Emx-1, Emx-2/ems</i>	Anterior patterning, cephalization	<i>Drosophila</i> , vertebrates
<i>Pax6/eyeless; Eyes absent/eya</i>	Anterior CNS/eye regulation	<i>Drosophila</i> , vertebrates
Polycomb group	Controls Hox expression/ cell differentiation	<i>Drosophila</i> , vertebrates
Netrins, Split proteins, and their receptors	Axon guidance	<i>Drosophila</i> , vertebrates
RAS	Signal transduction	<i>Drosophila</i> , vertebrates
<i>sine oculus/Six3</i>	Anterior CNS/eye pattern formation	<i>Drosophila</i> , vertebrates
<i>sog/chordin, dpp/BMP4</i>	Dorsal-ventral patterning, neurogenesis	<i>Drosophila, Xenopus</i>
<i>tinman/Nkx 2-5</i>	Heart/blood vascular system	<i>Drosophila</i> , mouse
<i>vnd, msh</i>	Neural tube patterning	<i>Drosophila</i> , vertebrates

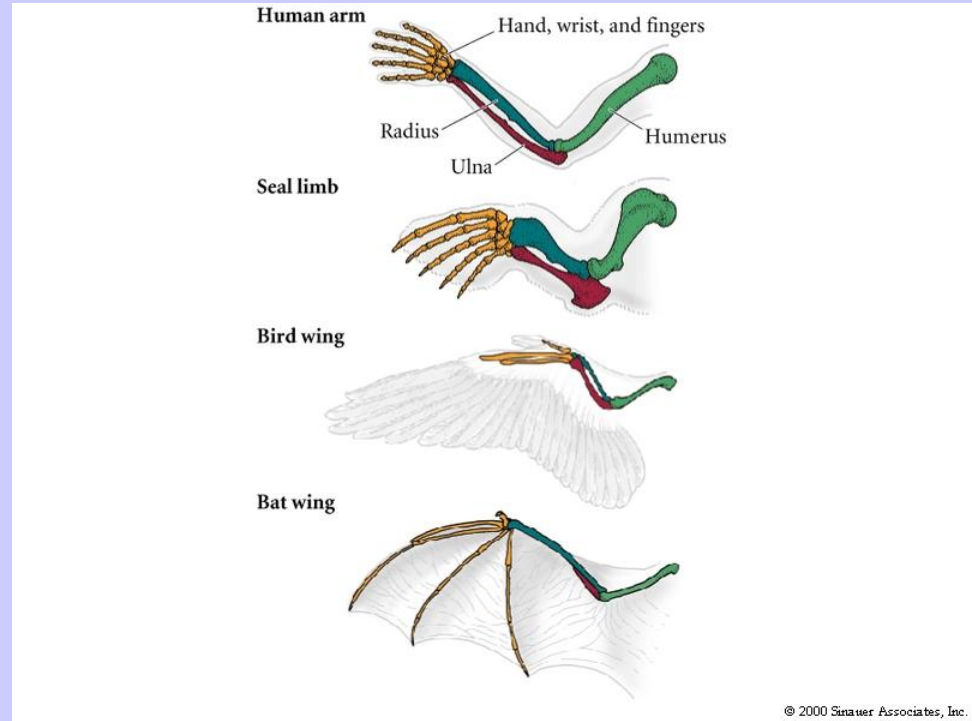
Source: After Erwin 1999.



# Homologies and Deep Homologies

# Homology and Analogy

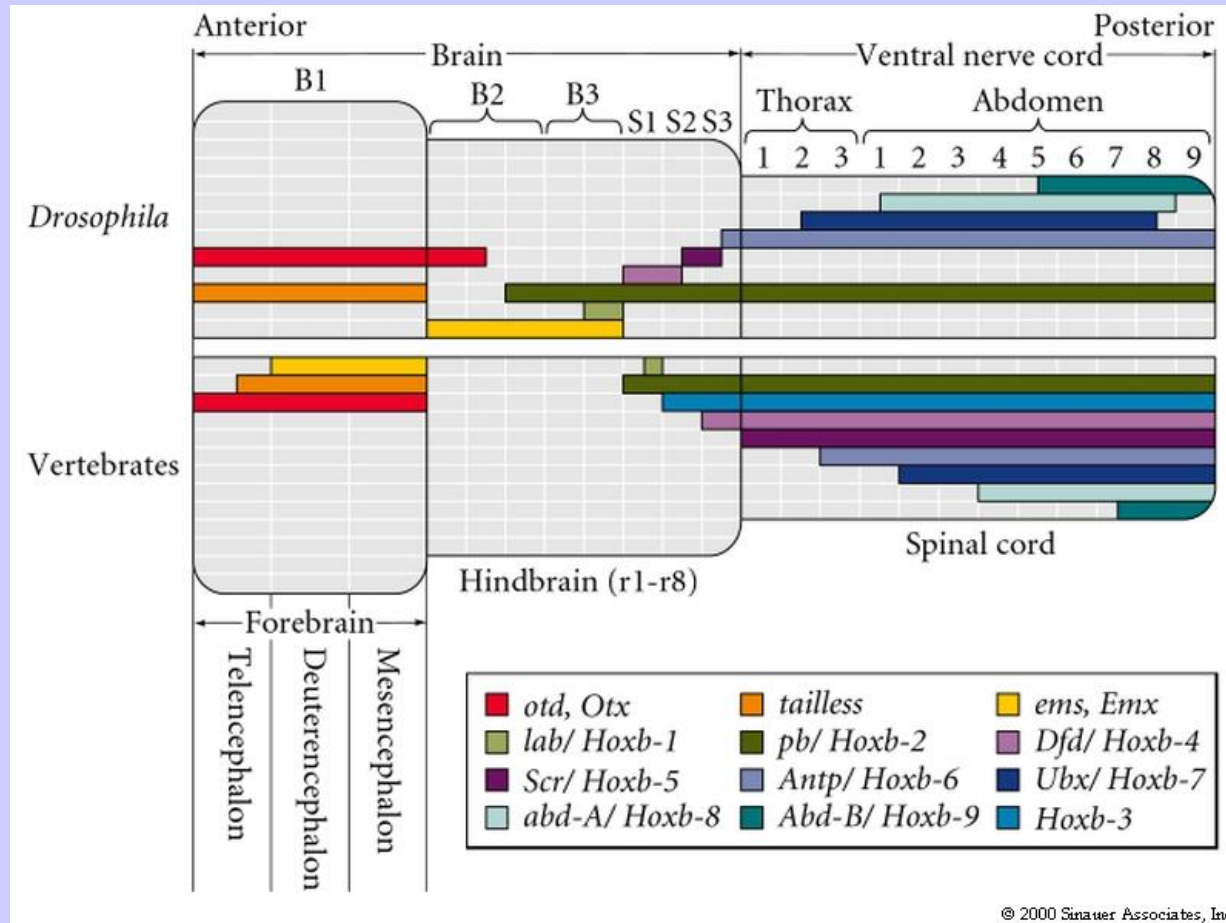
- Homology
  - similarity derives from common ancestry
  - vertebrate limb bones
- Analogy
  - similarity from performing similar function
  - butterfly and bird wings
- Genes or processes can also be either



# Deep Homology of *Hox* Genes

- Anterior-posterior specification
- Homologs
  - all animals
  - same order on chromosomes
  - same order of expression 3' = anterior
  - human *HOXB4* can substitute in flies for *deformed*

# A-P: Comparison of Regulatory Transcription Factors



# How Differ Between Phyla?

- Transcription factors
  - gene could change
  - could have different targets downstream
  - could be expressed in different pattern
    - within or
    - between body portions
  - could change in number

# Changing Regulatory Circuits

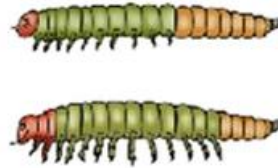
- Genes have many inputs and outputs
  - Genes have cis-regulatory elements which bind various transcription factors
  - Genes encode proteins (transcription factors)
- These are arranged in large, interacting networks
- Mutations
  - in cis elements potentially put the gene under new types of control by upstream regulators
  - in coding regions potentially allow the gene product to control new genes downstream

# How Can Hox Gene Changes Affect Morphology?

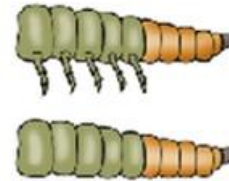
(A) Changes in Hox gene number



(B) Broad changes of Hox expression



(C) Subtle changes within Hox domains

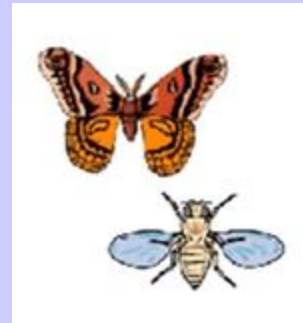


(D) Changes in regulation or function of downstream genes



# Downstream Responses (D)

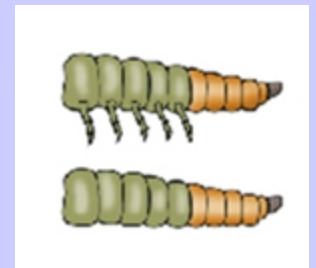
- Fruit fly
  - 2 wings, 2 halteres
- Butterfly
  - 4 wings
- Hox (Ubx) same expression pattern (in T3)
  - some genes down-regulated in *Drosophila* are not regulated by Ubx in butterflies
  - therefore escape (or acquire) (altered) regulation



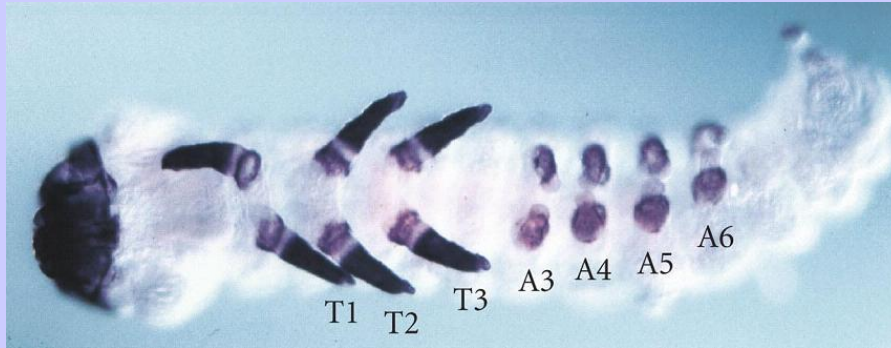


# Changes Within a Body Portion (C)

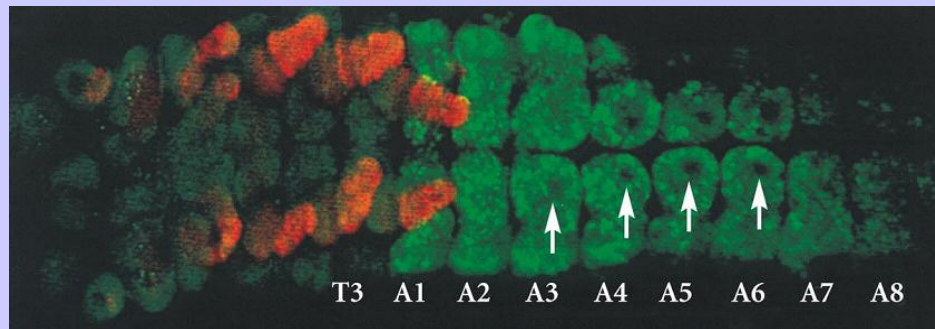
- *Distal-less* controls P-D axis of appendages
  - legs from each thoracic segment
  - not expressed in abdomen (*AbdA* and *Ubx* block)
- But in butterfly and moth larvae (caterpillars), *dll* is expressed in prolegs along abdomen
  - Down-regulation of *Ubx* and *abdA* in regions where *dll* then gets expressed



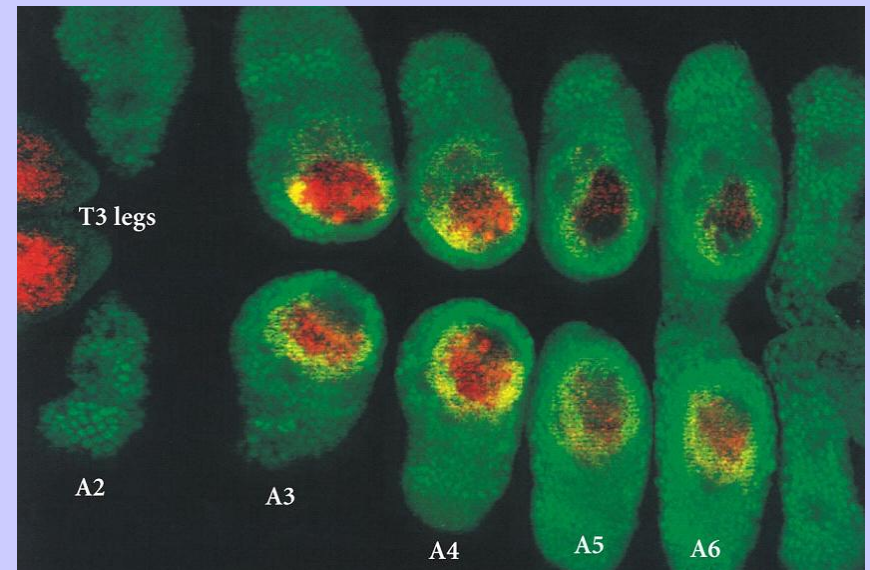
# Distal-less Expression



Dll (blue) in butterfly larva

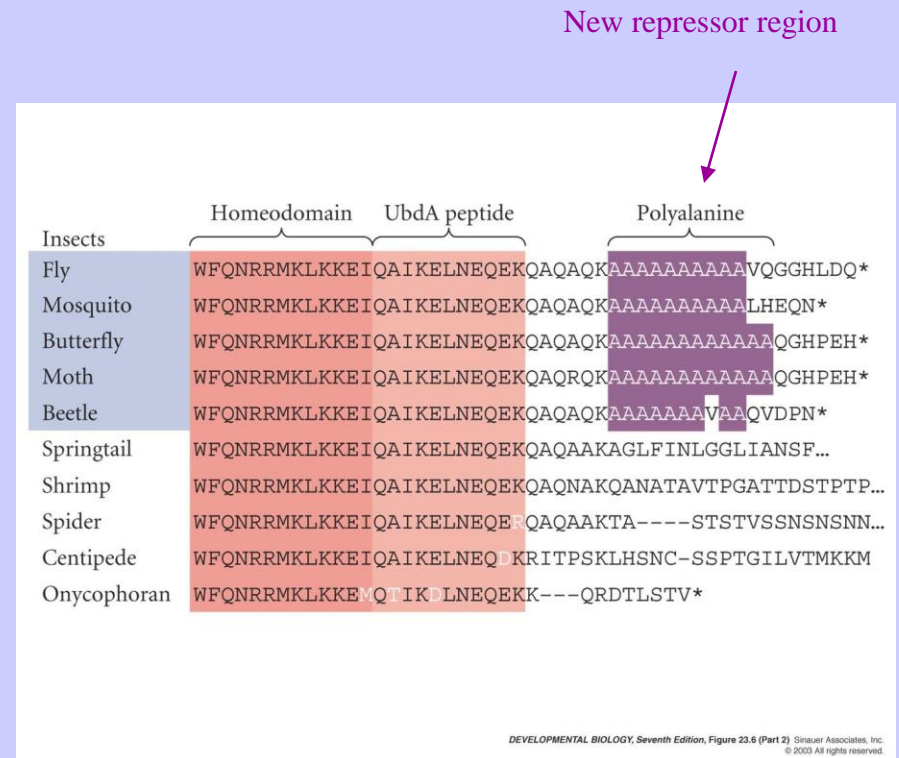


Dll (red)  
Ubx/AbdA (green)

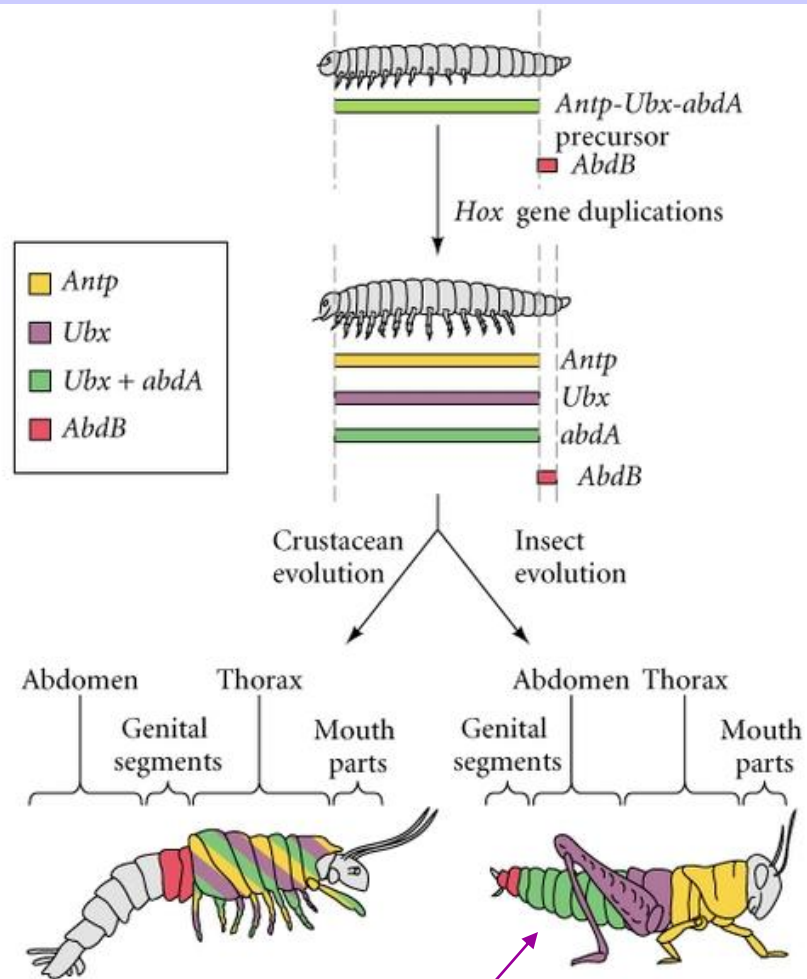


# Change in Gene Sequence

- Crustaceans (multiple legs)
  - all *thoracic* segments look the same
  - all express *Antp*, *Ubx*, *abdA* which don't repress *dll* in crustaceans
- Different in insects (6 legs)
  - *Ubx* gained a region that can repress *dll*



# Result



legs repressed

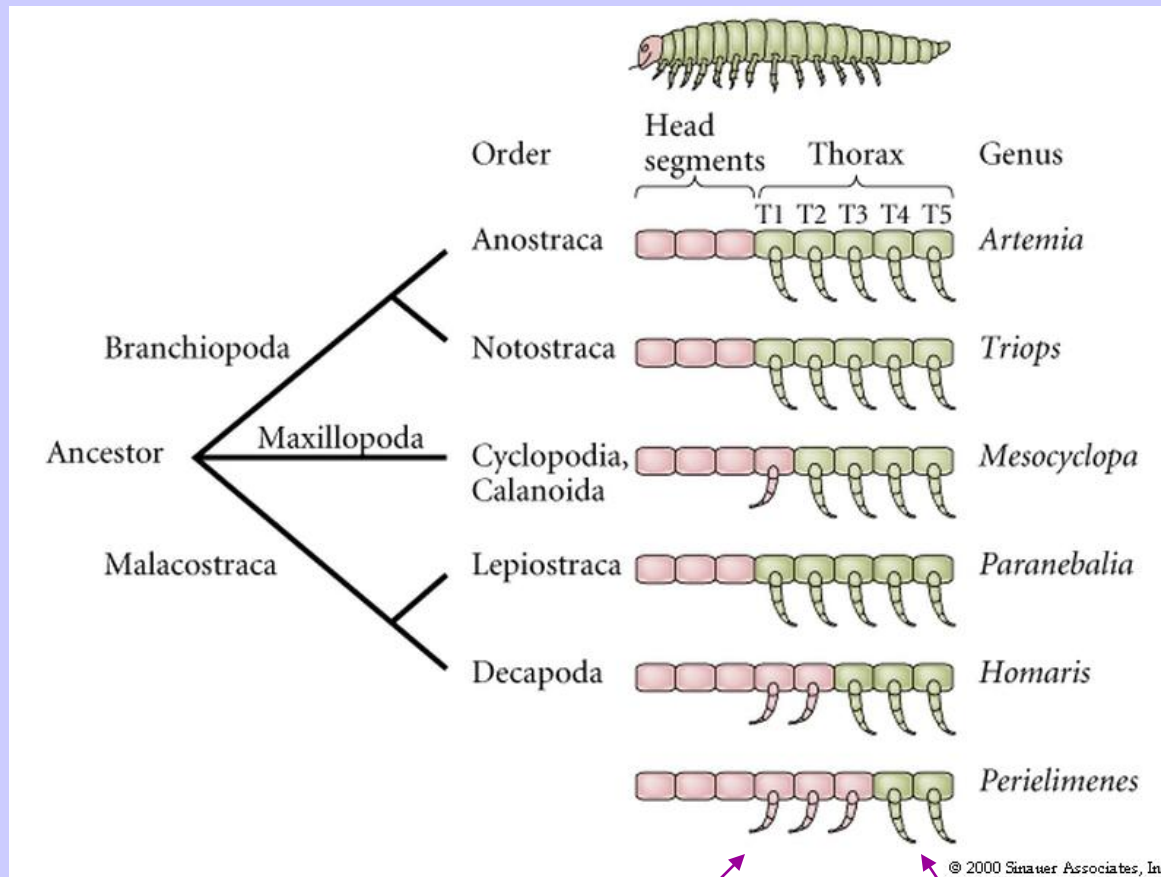
# Changes Between Body Segments (B)



- If both *Ubx* and *abdA* are expressed in thorax segment, crustacean makes “legs”
- If neither, makes maxilliped (feeding appendage)
  - e.g. brine shrimp have no maxillipeds
  - lobsters have maxillipeds in T1 and T2

# *Ubx* and *AbdA* in Crustaceans

green=*Ubx/abdA*



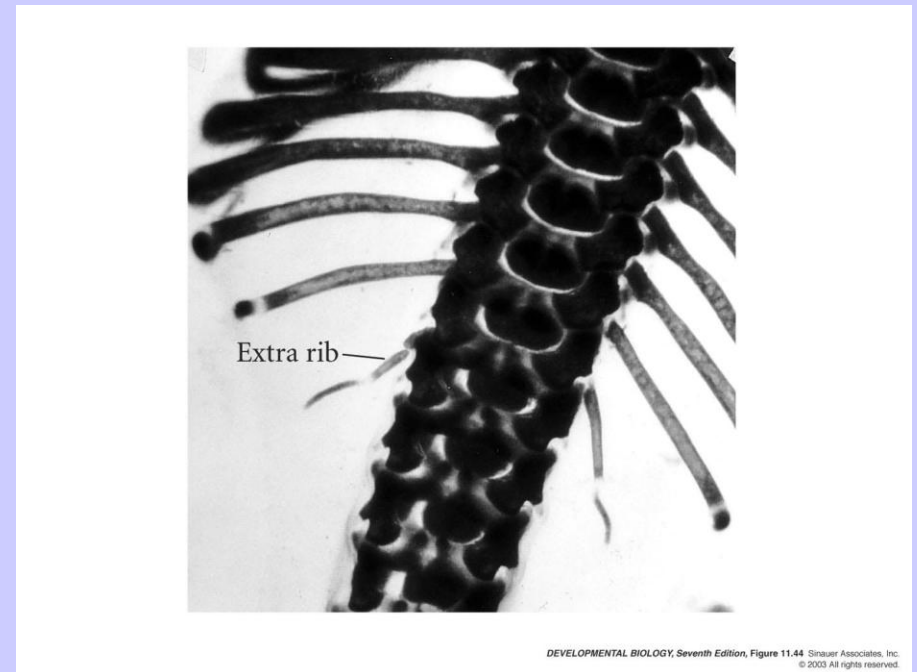
maxilliped

leg

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# Vertebral Patterns Controlled by Hox Genes

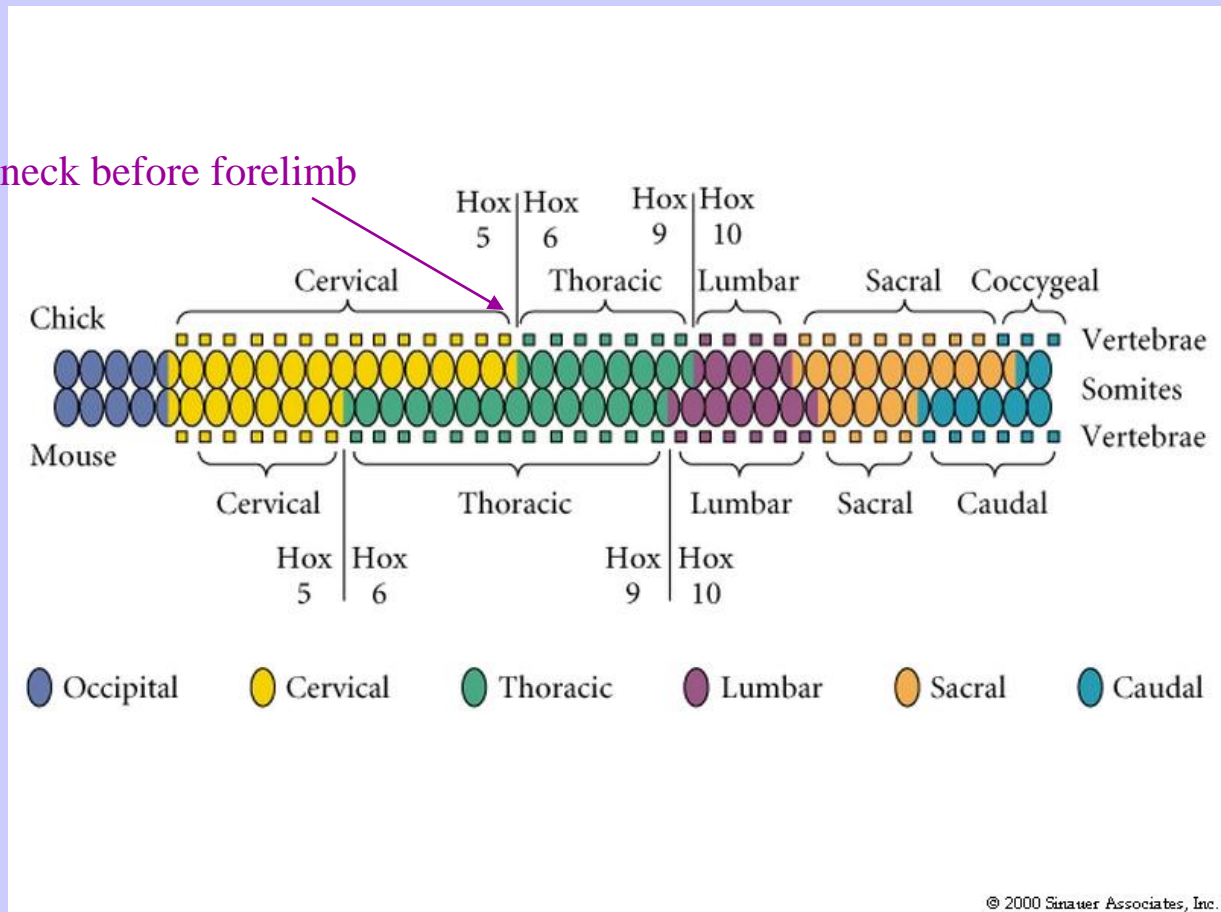
- *Hox* pattern determines type of vertebrae
  - cervical-thoracic (ribbed) -lumbar-sacral-caudal
- KO *Hoxc-8* in mouse
  - L1 forms rib like T12





# Hox Patterns Shifted in Chick and Mouse

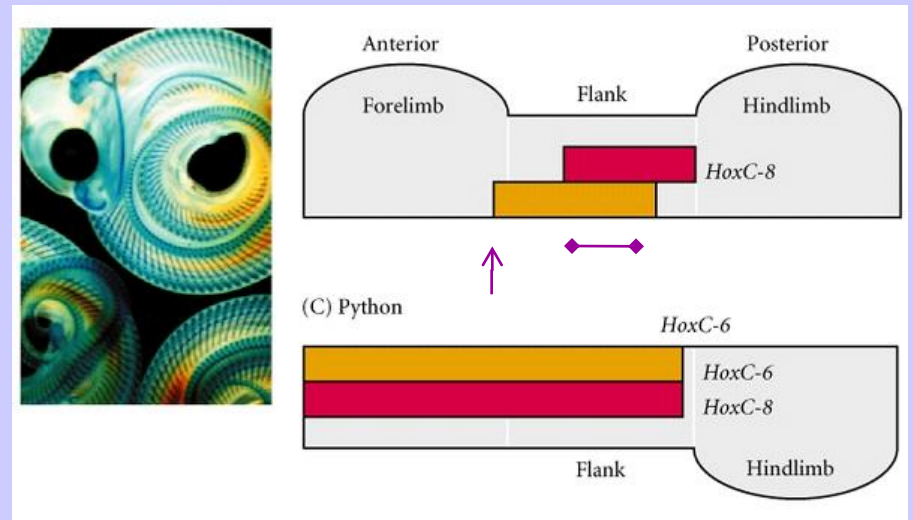
Long neck before forelimb





# Loss of Forelimb in Snakes

- Evolve from lizards, lose legs
  - forelimb forms anterior to most anterior expression of *Hoxc-6*
  - then *Hoxc-6* and *Hoxc-8* determine T (rib) segments
  - in snakes no segment has only *Hoxc-6*, all ribs



# Changes in *Hox* Number (A)

- Sponges have only a few *Hox* genes
- More complex invertebrates have a single cluster of ~ 7
- Invertebrate deuterostomes have one similar cluster
- Two duplications in vertebrates → 4 clusters
  - accompanied by neural crest, new cell types and spinal cord and brain
  - affect segmentation of nervous system and somite derivatives (bone *and* muscle)
  - hypothesis: divergence allows more functions

