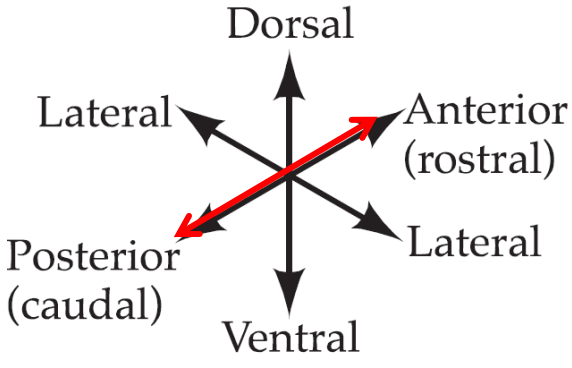
# Part 2, Nervous System Development and Diseases

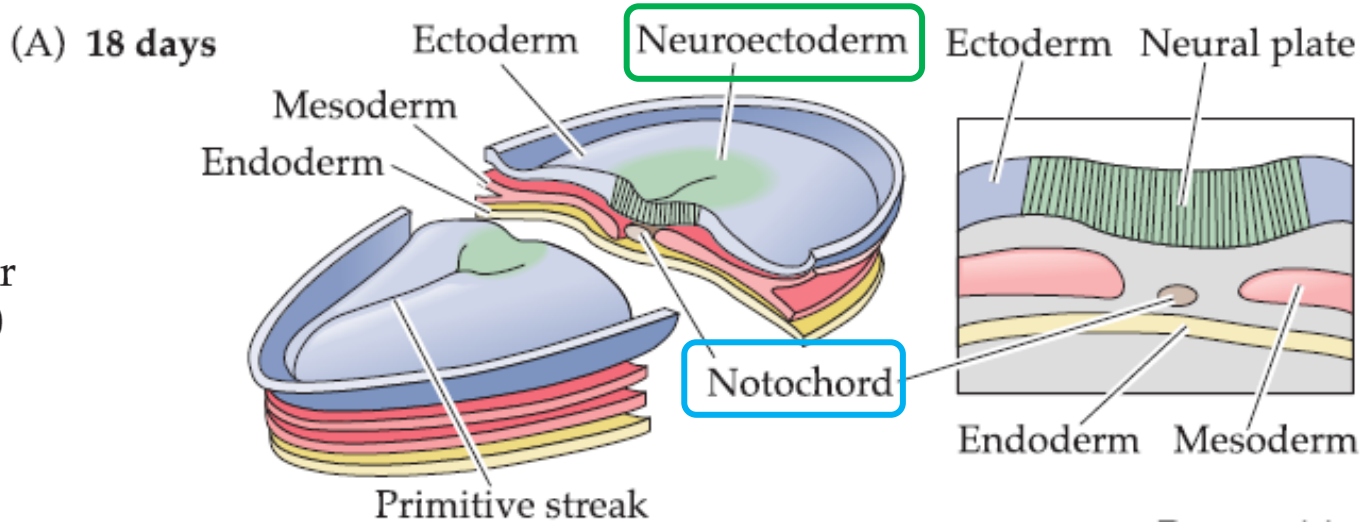
## 2.1. Early nervous system development

# Formation of nervous system

## ❖ Gastrulation

- **Local invagination: three germ layers**
  - Outer ectoderm
  - Middle mesoderm (initiating invagination)
  - Inner endoderm
- **Establishment of the midline and the basic body axes**
- **Formation of notochord at the midline: central event**
  - **Notochord**: distinct cylinder of mesodermal cells
  - Notochord defines embryonic midline and is the axis of symmetry for the entire body
  - **Neuroectoderm**: lies immediately above the notochord and gives rise to the entire nervous system
  - **Notochord**: transient structure that disappears once early development is complete

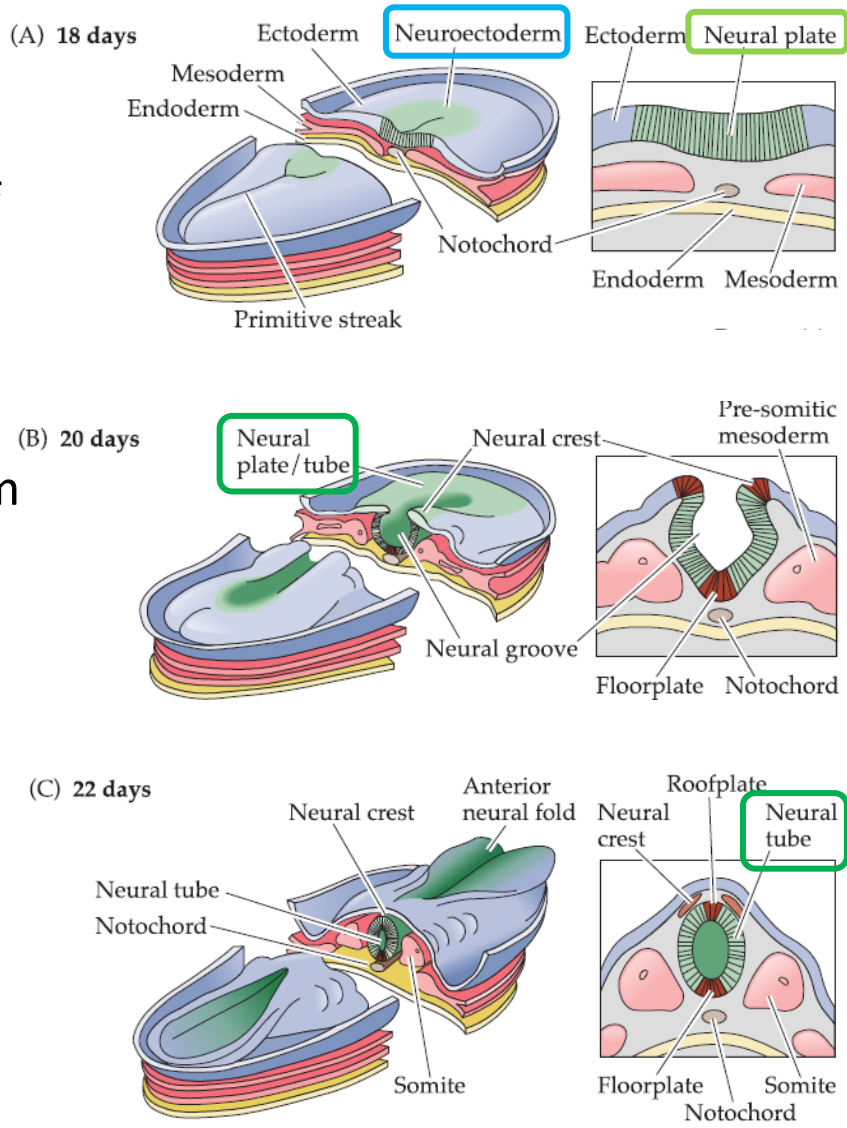


# Formation of nervous system

## ❖ Neurulation

- Notochord sends inductive signals to the overlaying ectoderm that cause a subset of cells to differentiate into **neuroectodermal precursor cells.**
- Midline ectoderm containing these cells thickens into a distinct columnar epithelium called **neural plate**.
- The lateral margins of the neural plate fold inward, transforming the neural plate into a tube—**neural tube**.
- The cells in **neural tube** gives rise to the brain, the spinal cord and most of PNS.



# Neural stem cells

- **Neuroectodermal precursor cells**: **neural stem cells**
  - Dividing to produce more precursor cells (self-renewal)
  - Capable to give rise to the full range of cell classes

- Differentiation order

Subsets of neuroectodermal precursor cells (**stem cells**)

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Region- and fate-specified neural **progenitors**

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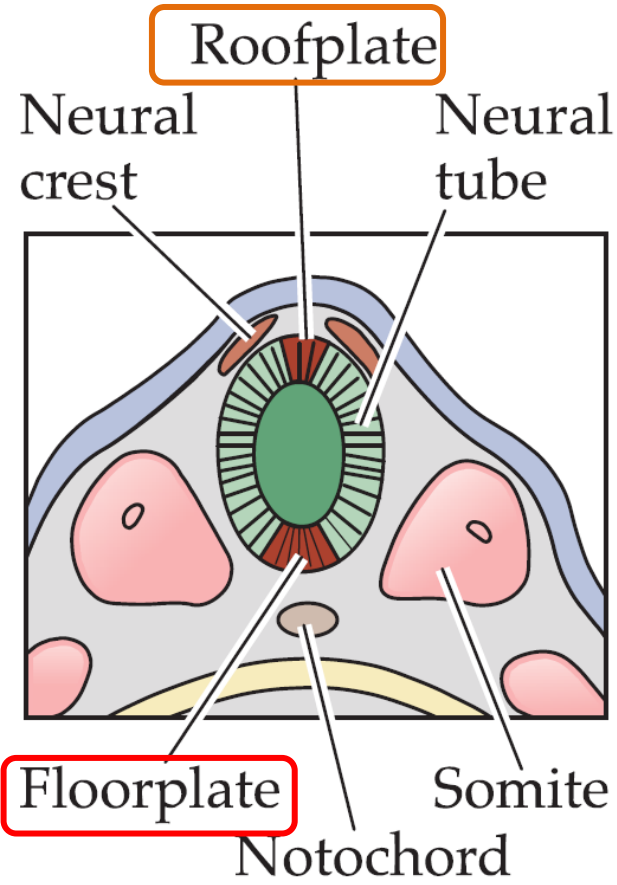
Specific classes of **neurons**, and also **astrocytes**, **oligodendroglial cells**

# Floor plate and roof plate

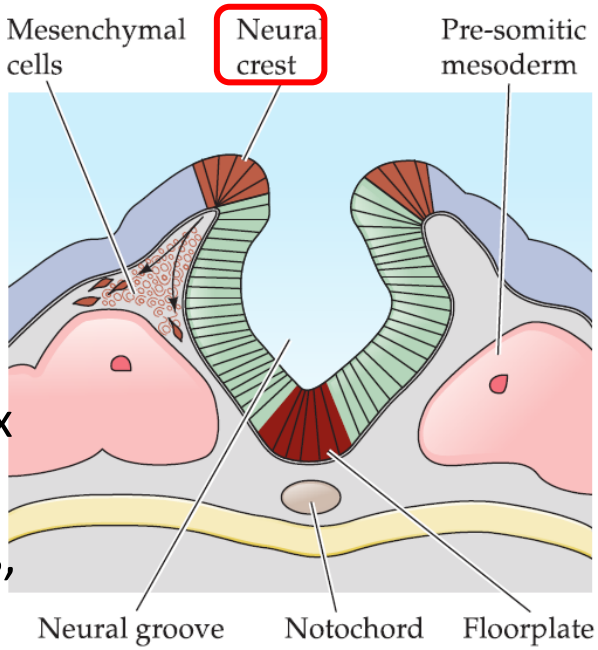


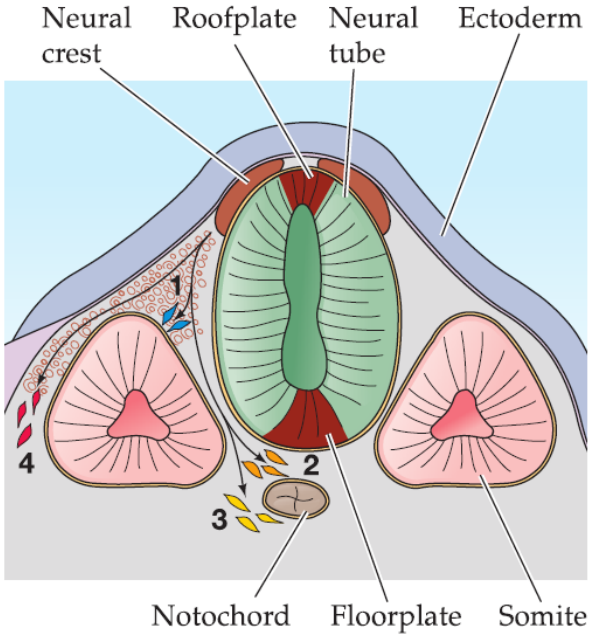

- **Floor plate**: specialized strip of epithelial-like cells at the ventral midline of the neural tube. Sequential functions as follows:
  - Molecular signals from the **floor plate** as well as from the **notochord** specify position and fate for the neuroectodermal precurcors of the *spinal cord* and *hindbrain*.
  - These signals lead to differentiation of cells in the ***ventral*** portion of the neural tube that eventually give rise to spinal and hindbrain motor neurons and related interneurons (details later on).
- **Roof plate**: narrow strip of neuroepithelial cells at the dorsal midline of the neural tube.
  - Molecular signals from the **roof plate** help define position and fate for the interneurons in the more ***dorsal*** regions of the *spinal cord* and *hindbrain* (details later on).

# Neural crest

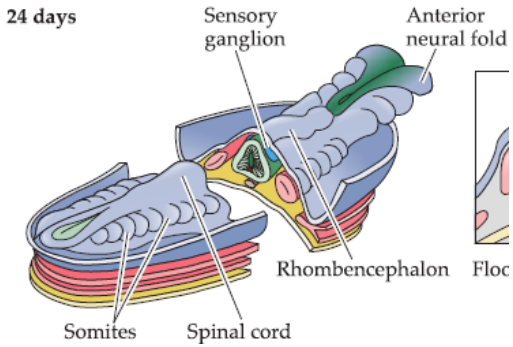
- **Neural crest**: the region where the edges of the folded neural plate come together.
- **Neural crest cells**: a *third* population of precursor cells.
  - Migrating away from the neural tube through a matrix of loosely packed mesenchymal cells.
  - Subsets of neural crest cells follow different pathways, along which they are exposed to additional signals that influence their specific differentiation, and give rise to:

1. Neurons and glia of the sensory ganglia.
2. Neurons and glia of the visceral motor (autonomic) ganglia.
3. Neurosecretory cells of the adrenal gland which eventually aggregate around the dorsal portion of the kidney.
4. Non-neural structures such as pigment cells, cartilage, and bone, particularly in the face and skull.



# Formation of major brain subdivisions

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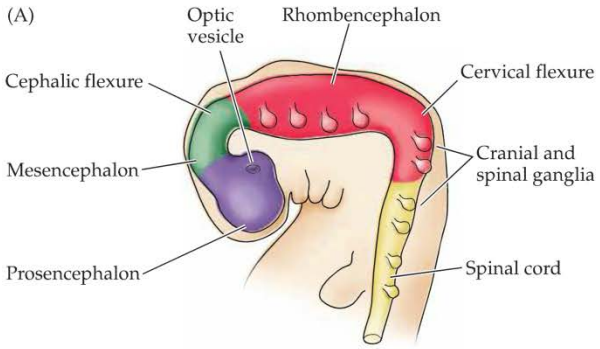
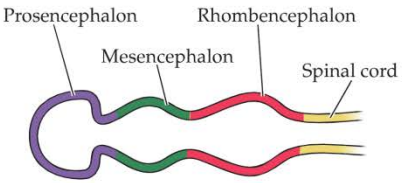
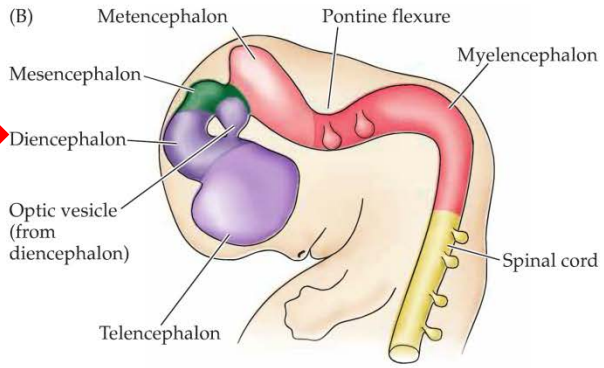
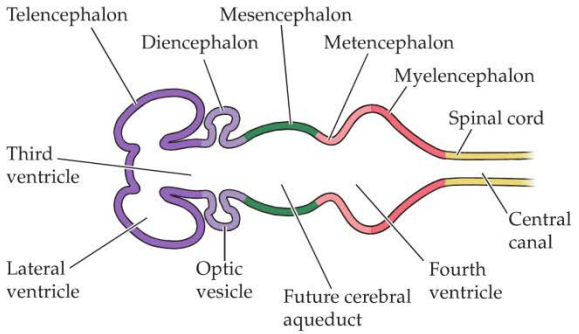
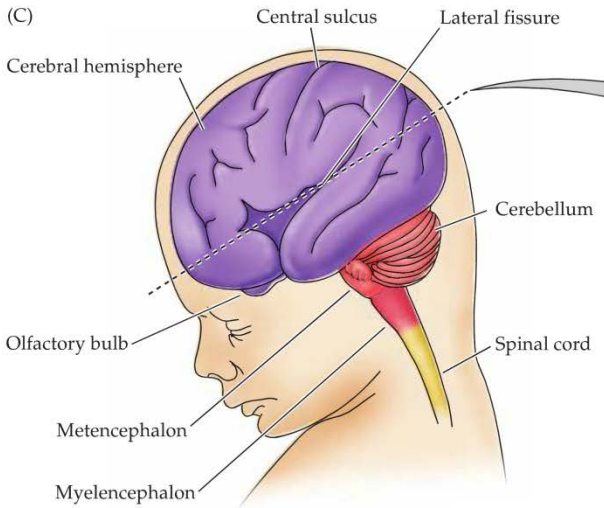
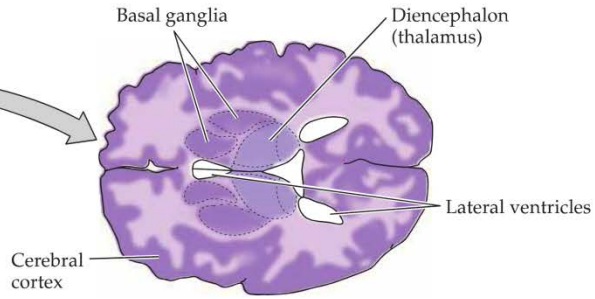


# Segmentation

- The neural tube is organized into repeating units called **neuromeres**.

- **Segmentation**: establishing regional identity in the body by dividing the embryo into repeated units, or segments.

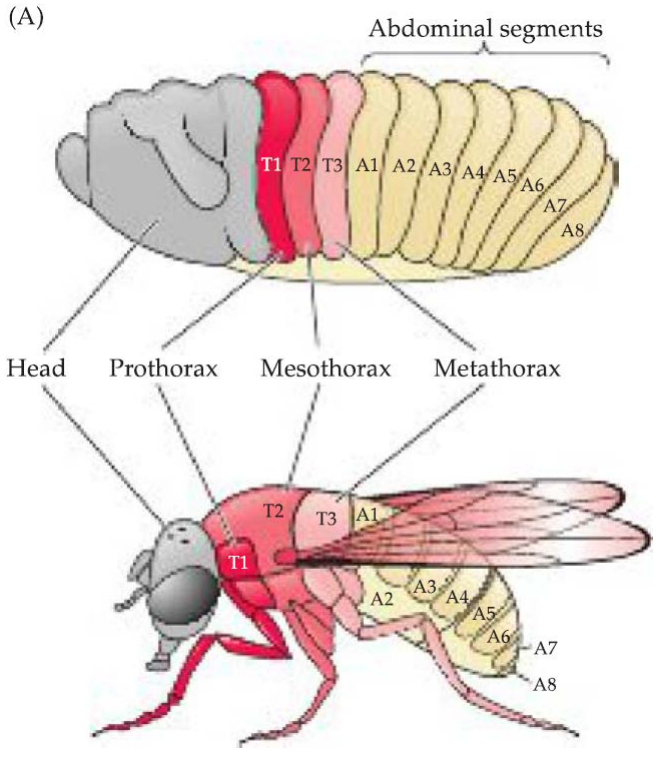
- **Fruit fly *Drosophila***: early expression of **homeotic** or **homeobox** genes guides the differentiation of the embryo into distinct segments that give rise to the head, thorax, and abdomen.
  - Temporal pattern of expression of four homeobox genes encoding TFs.

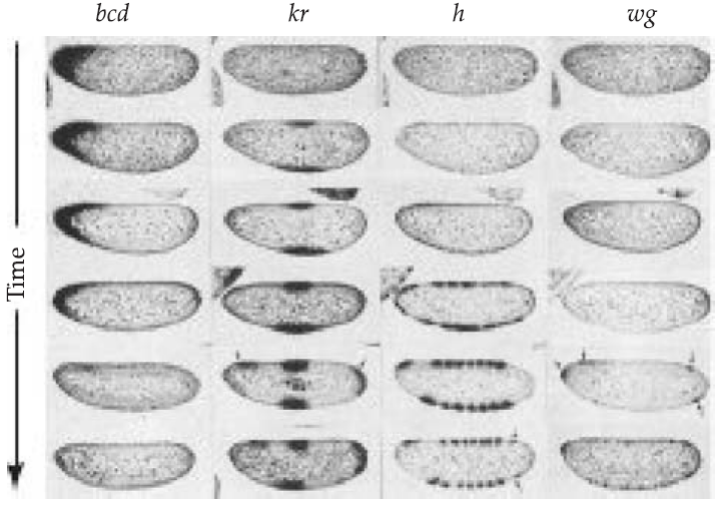
***bcd***: defining the anterior pole of the embryo.

***kr***: expressing in the middle and then at the posterior end of the embryo, defining the anterior-posterior axis.

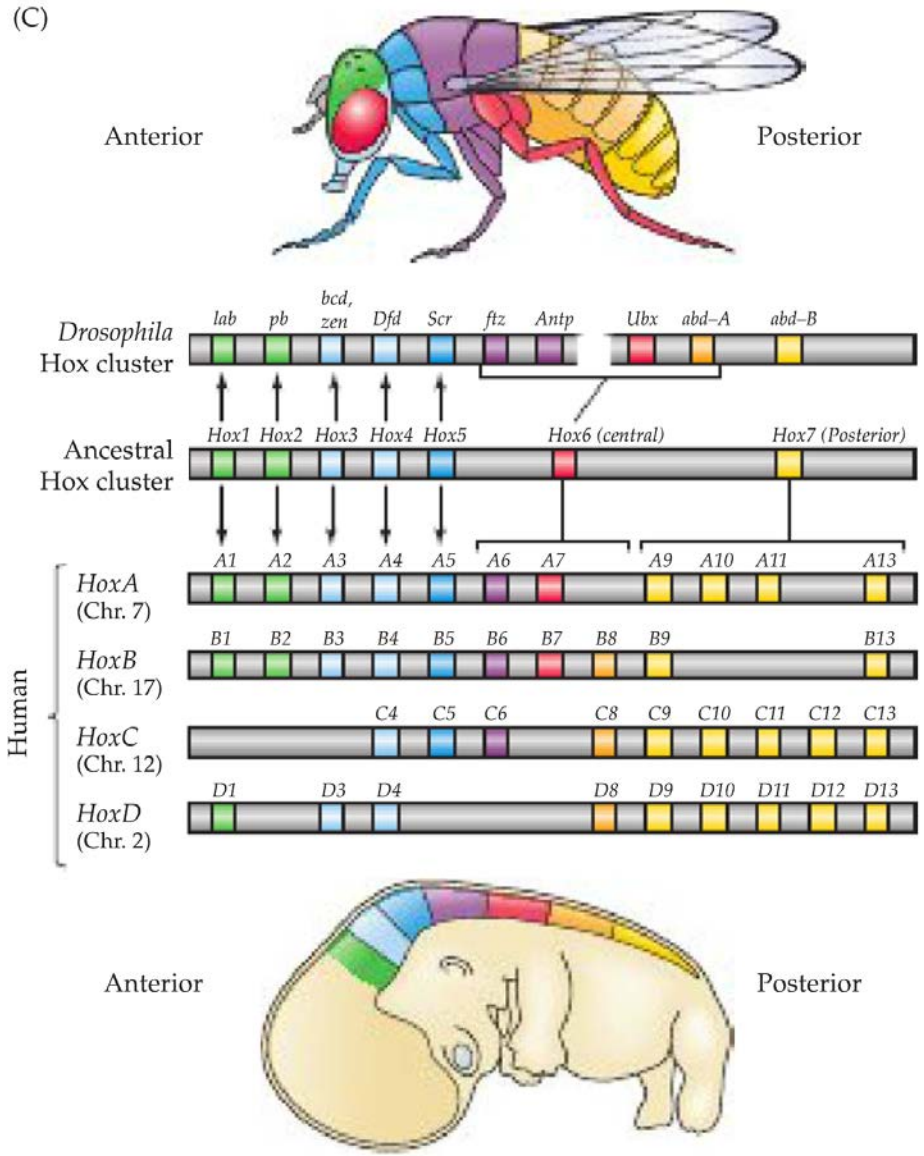
***h***: delineating the domains that will eventually form the mature segmented body.

***wg***: further refining the organization of Individual segments.



# Parallels between *Drosophila* and human *Hox* genes




- Human *Hox* genes (and those of most mammals) have been duplicated twice, leading to four Independent groups (**A, B, C, D**), each on a distinct human chromosome.

- The anterior-to-posterior pattern of *Hox* gene expression in both flies and mammals follows the 5'-to-3' orientation of these genes on their respective chromosomes.