

# The later development in xenopus and zebrafish

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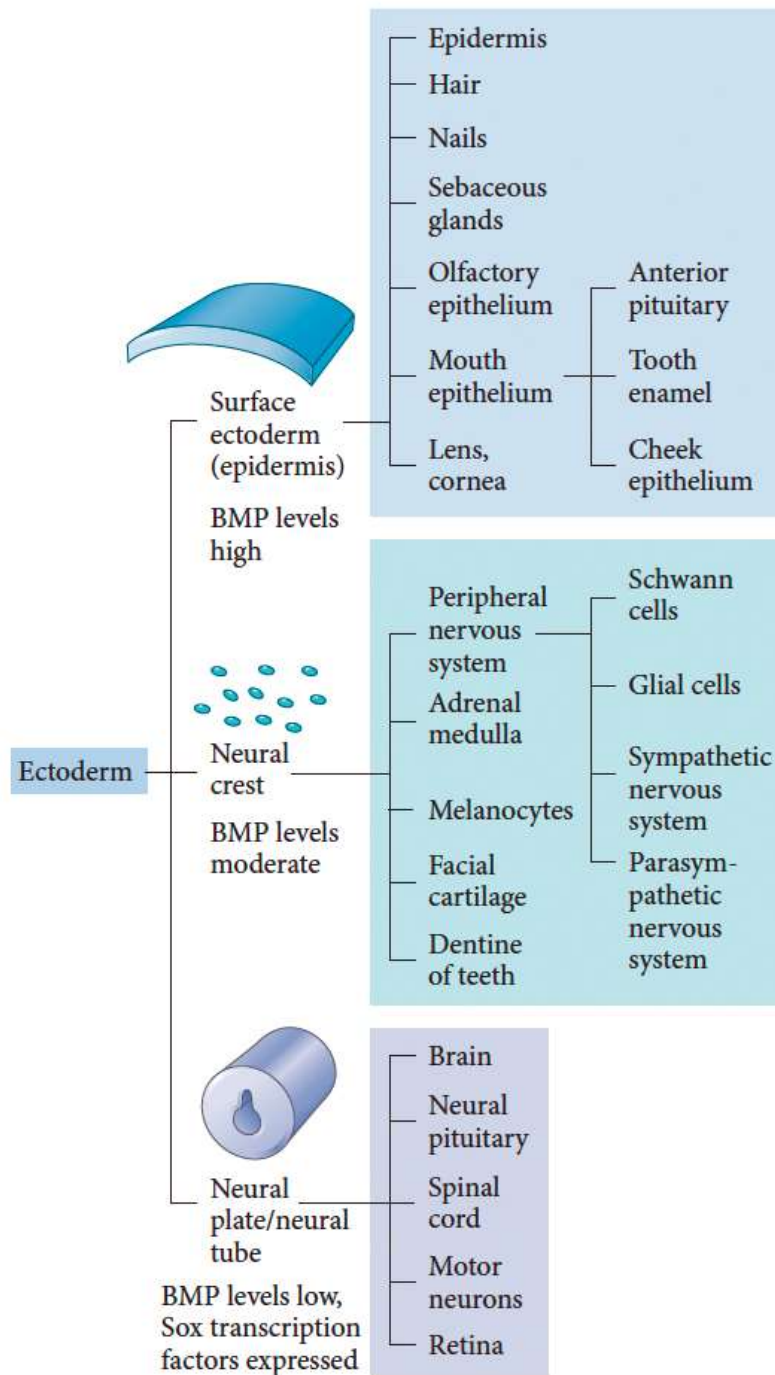


**Xenopus: gastrulation~ neurulation**

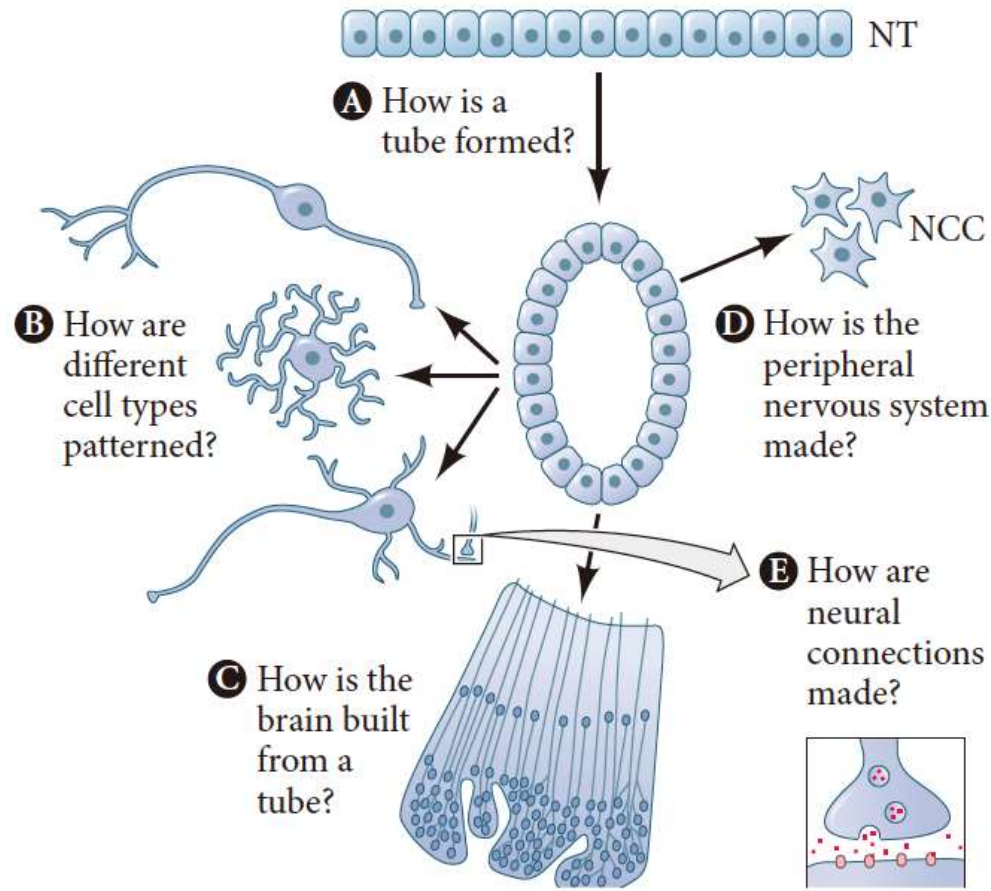
# outline

- Ectoderm
  - 1) neural tube formation and differentiation
  - 2) neural crest cells
  - 3) eye development
- Mesoderm
  - 1) paraxial mesoderm: somite
  - 2) intermediate mesoderm: kidney
  - 3) lateral plate mesoderm: heart, blood vessels, blood cells
- Endoderm
  - gut

# Major derivatives of ectoderm germ layer



# The major questions to be addressed during ectoderm differentiation

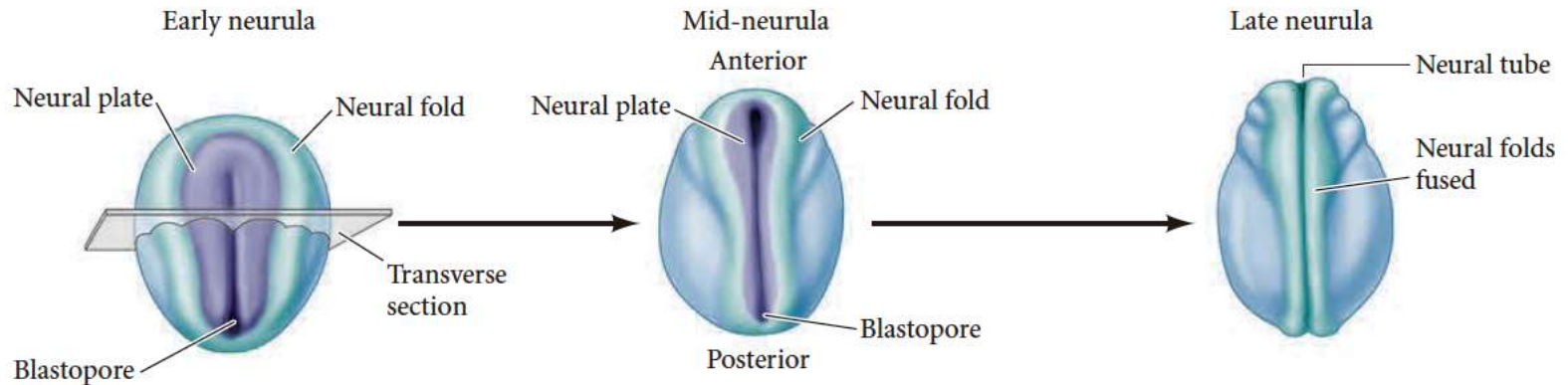


# outline

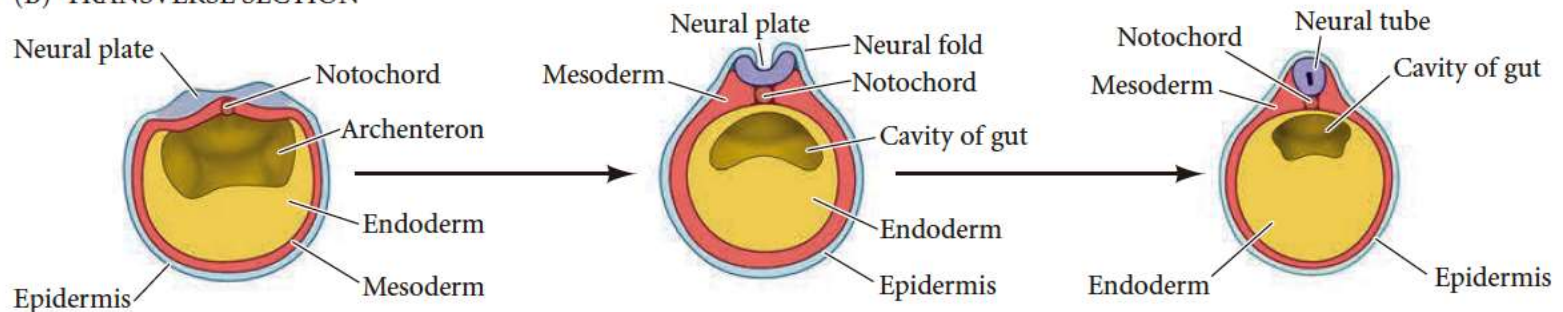
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# Primary neurulation in an amphibian embryo

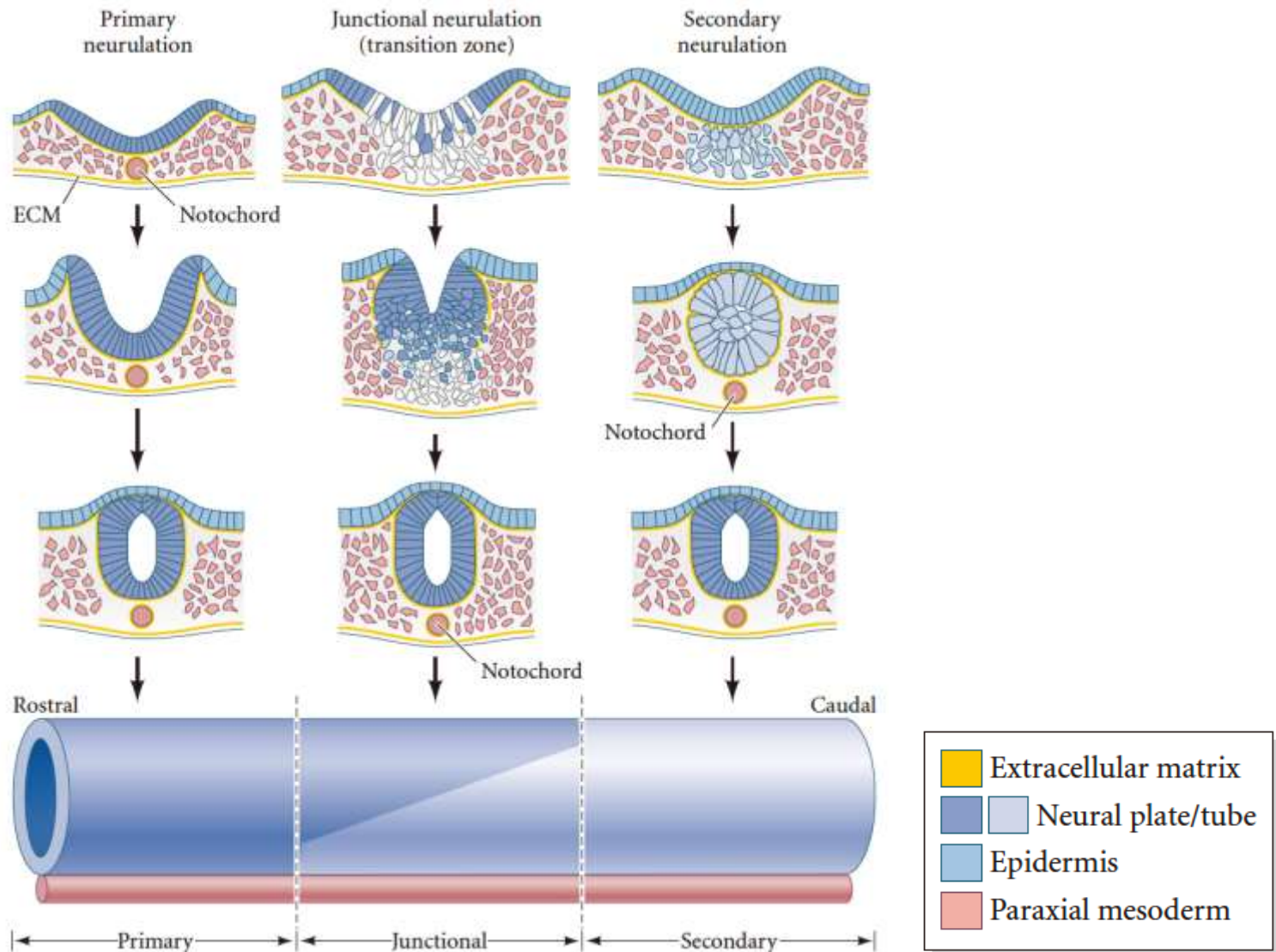
(A) DORSAL SURFACE



(B) TRANSVERSE SECTION



# Primary vs secondary neurulation

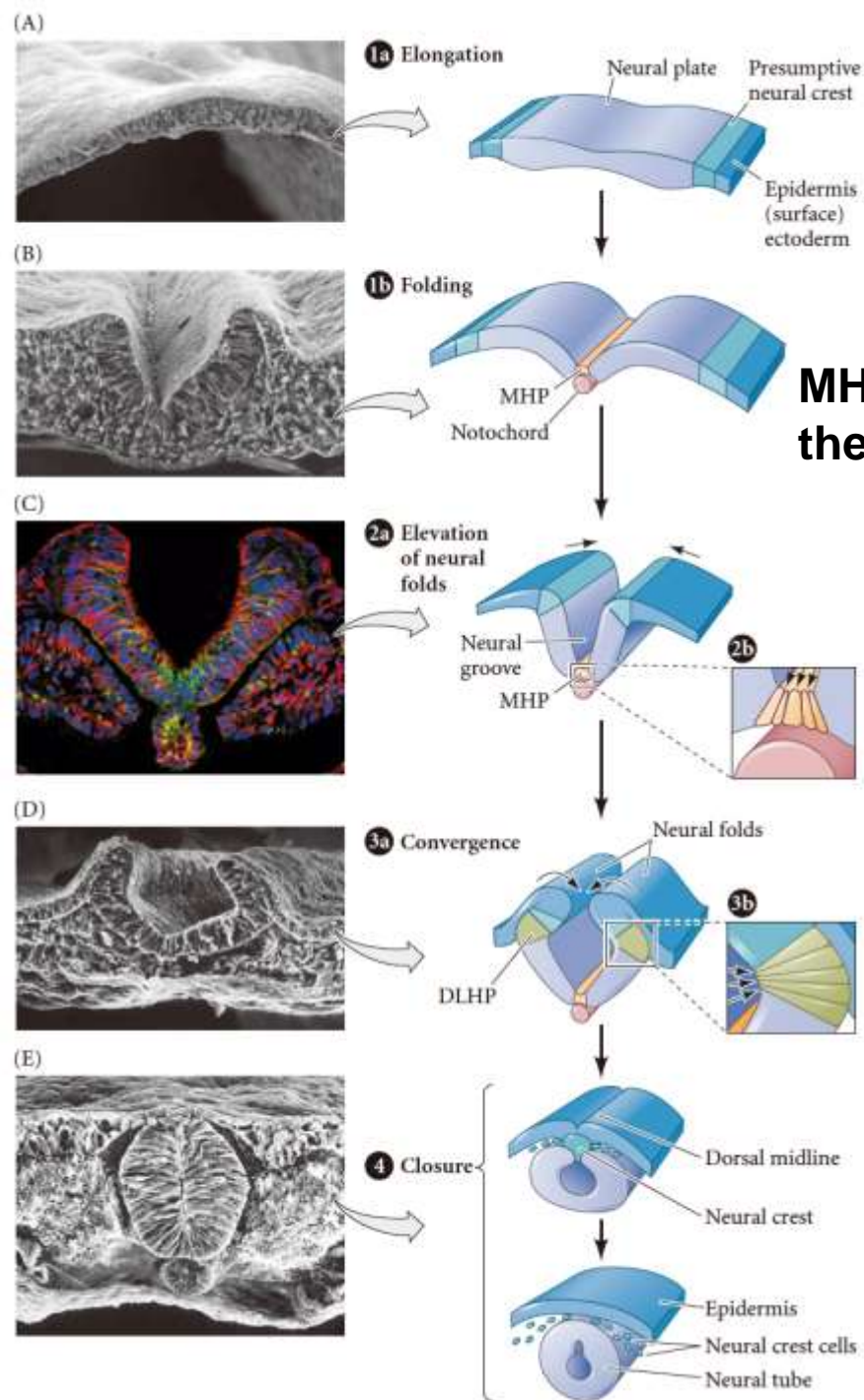




# Neural tube (神经管) formation

- **neural tube (神经管)** is the rudiment (原基) of the central nervous system, the formation process of which is called neurulation (神经管形成). There are two major ways of neurulation: primary (初级) neurulation and secondary (次级) neurulation.
- **Primary neurulation:** neural plate cells → proliferate, invaginate and pinch off → tube (anterior)
- **Secondary neurulation:** mesenchyme cells → coalescence (聚集) → cord → hollow → tube (posterior)

# Primary neurulation in chick embryo

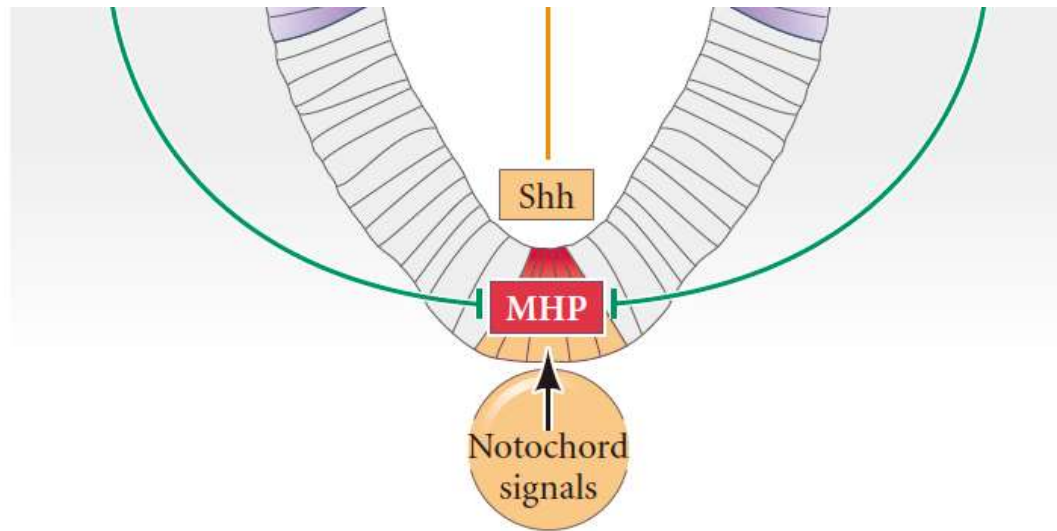


**MHP:**  
the medial hinge point

**“wedge-shaped”**  
(楔形)

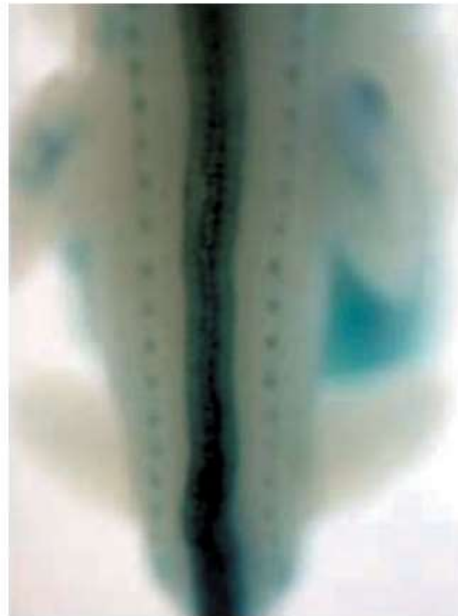
**DLHP:**  
the dorsolateral hinge point

# Notochord and its secreted Shh is required for MHP formation



# Noggin is required for DLHP and neural tube closure

(A) Wild-type



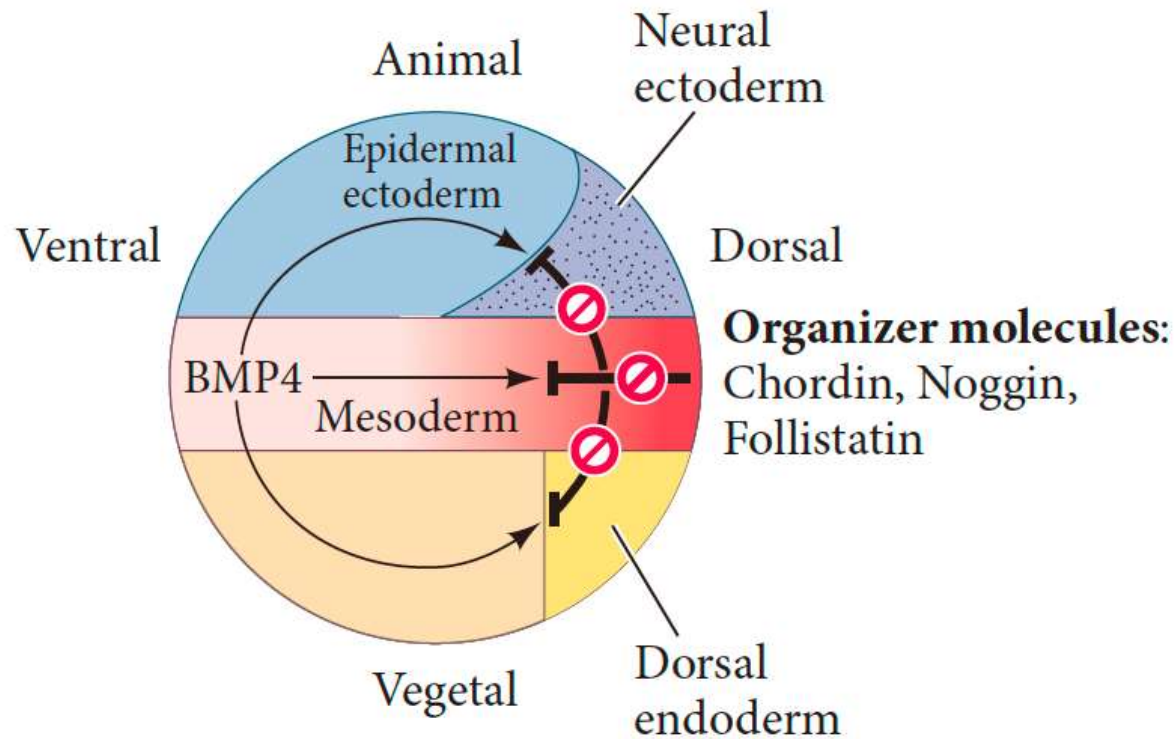
*Noggin* expressed;  
neural tube closure

(B) *Noggin*<sup>-/-</sup>

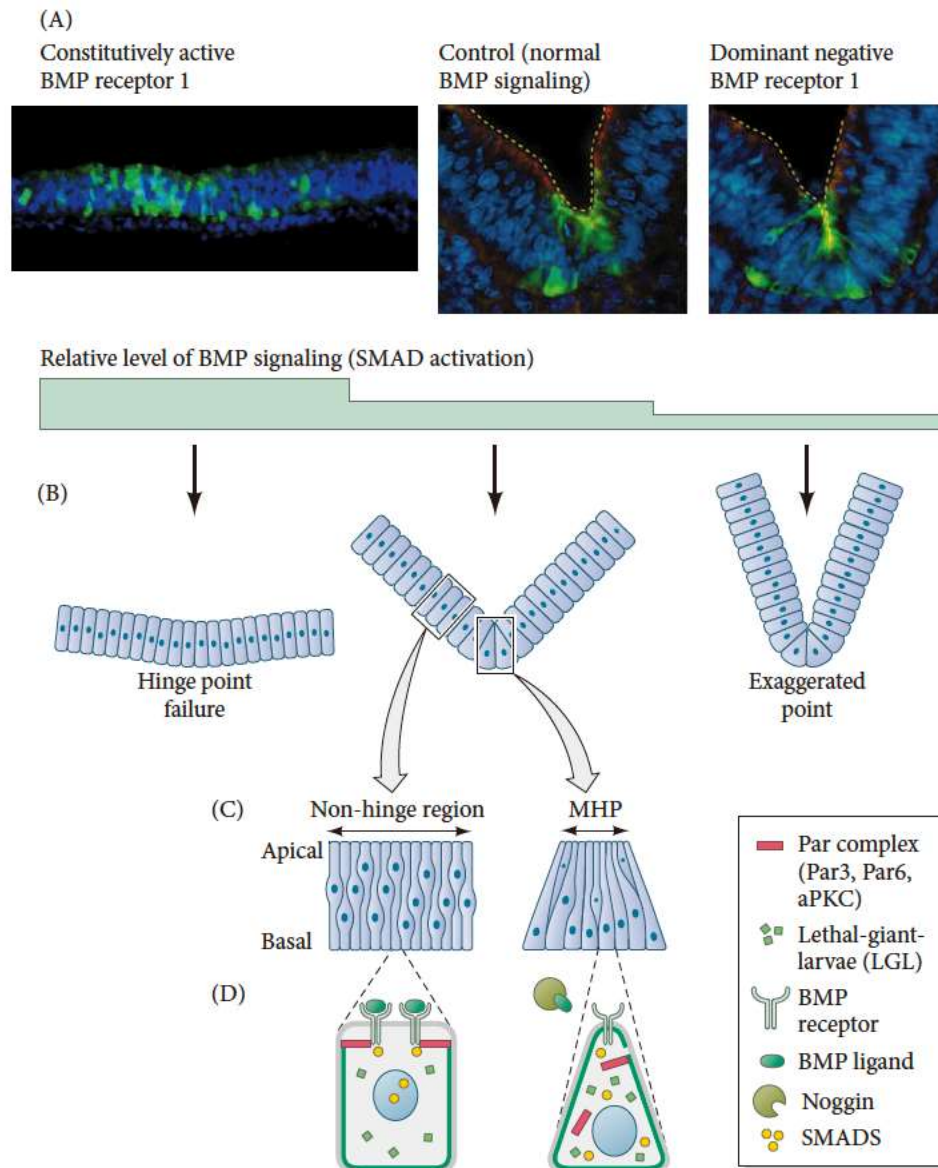


BMPs hyperactive,  
neural tube fails to close

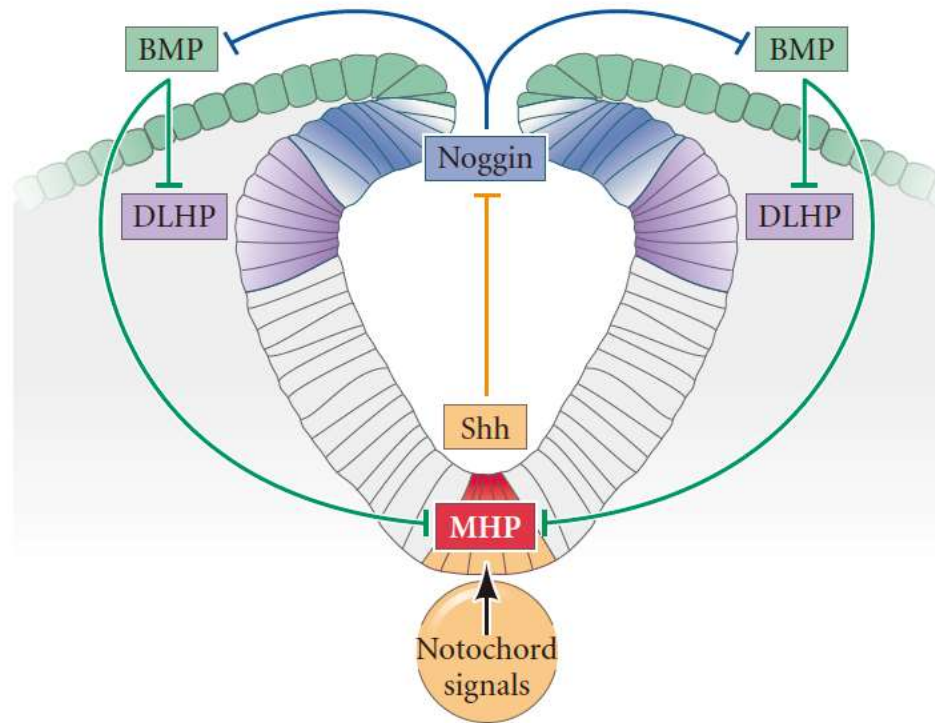
# Mechanism of organizer's function in DV patterning



# BMP prevents MHP formation



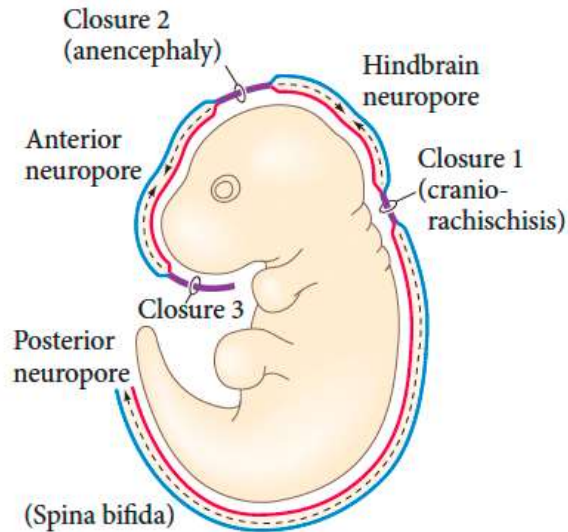
# Morphogen regulation of hinge point formation



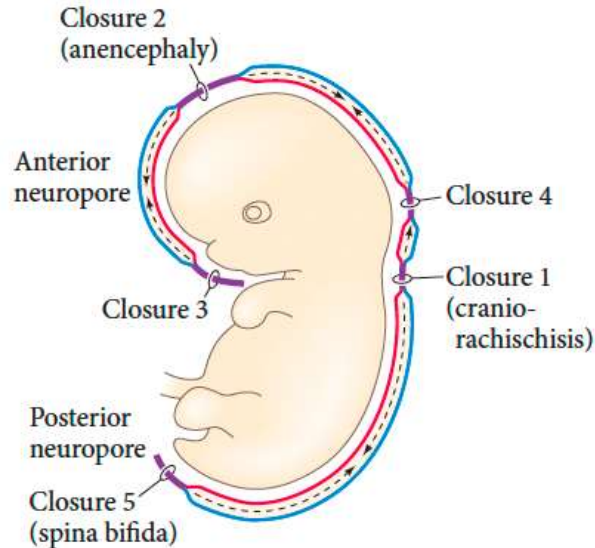


# Neural tube closure in the mammalian embryo

(A) MOUSE



(B) HUMAN



(F)



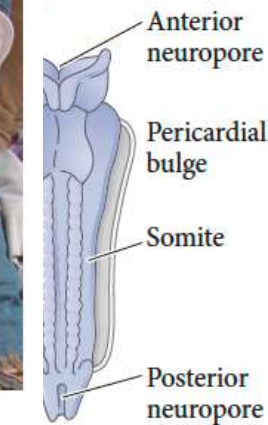
Exencephaly; spina bifida

22 days

(G)



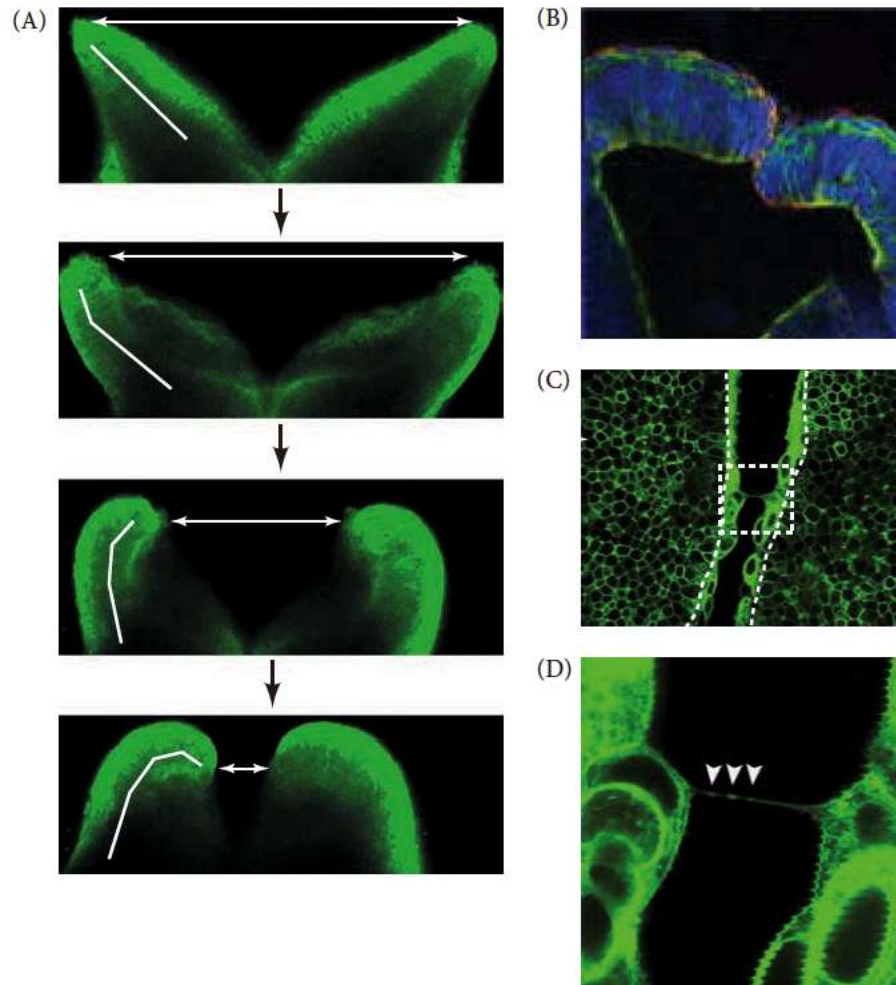
Anencephaly



23 days

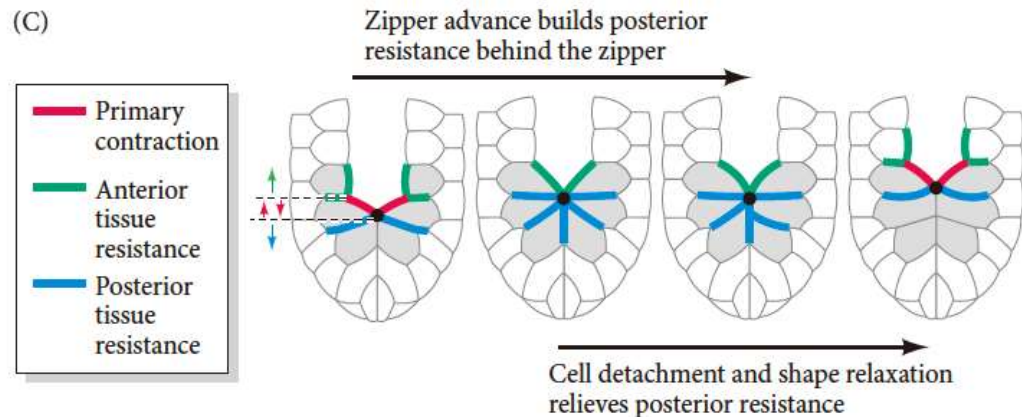
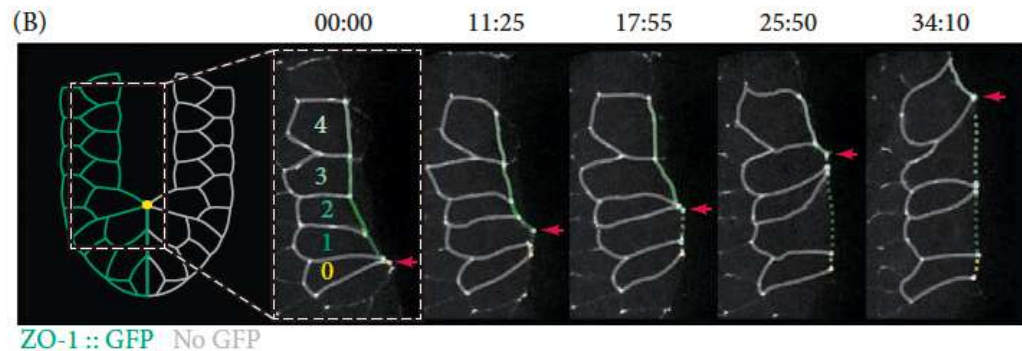
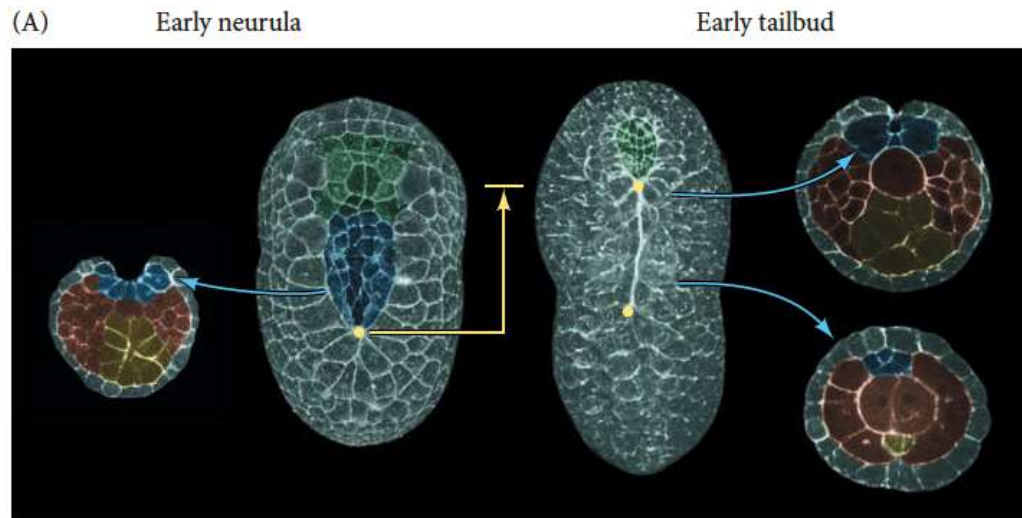


# Neural tube closure at mouse site 2 (midbrain region)



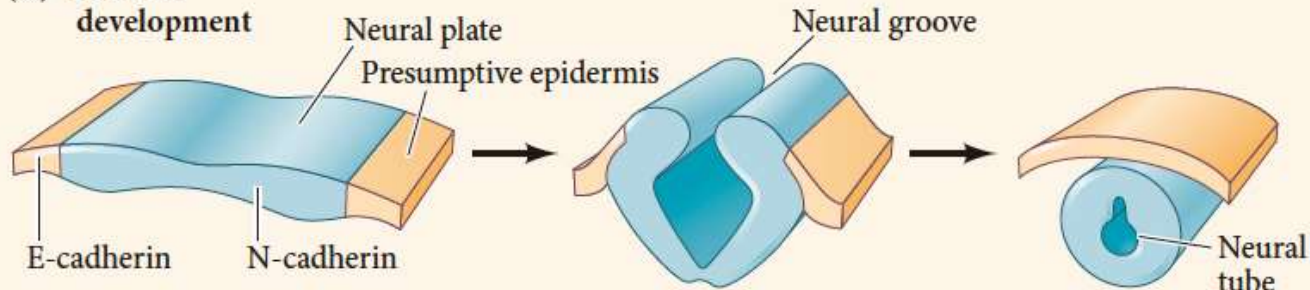
a transgenic  
CAG:Venusmyr mouse

# Neural tube zipper advance in *Ciona* (海鞘)

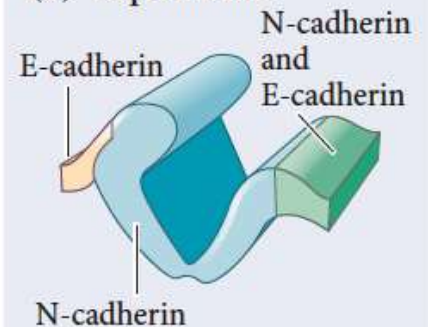


# Expression of N- and E-cadherin adhesion proteins during neurulation in *Xenopus*

(A) Normal development

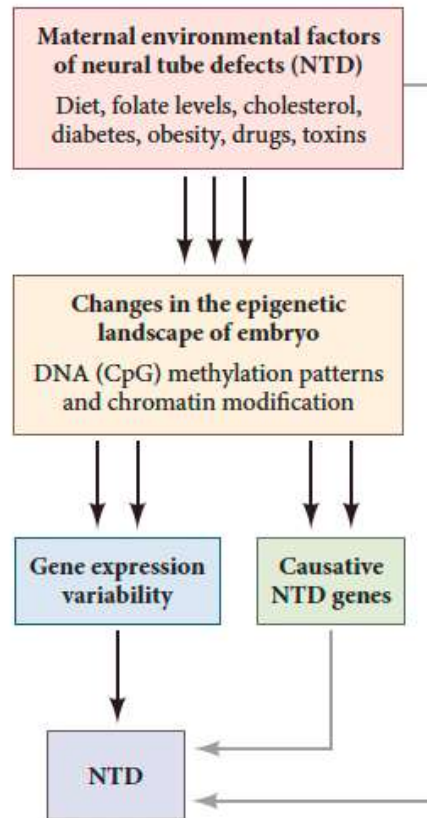


(B) Experimental

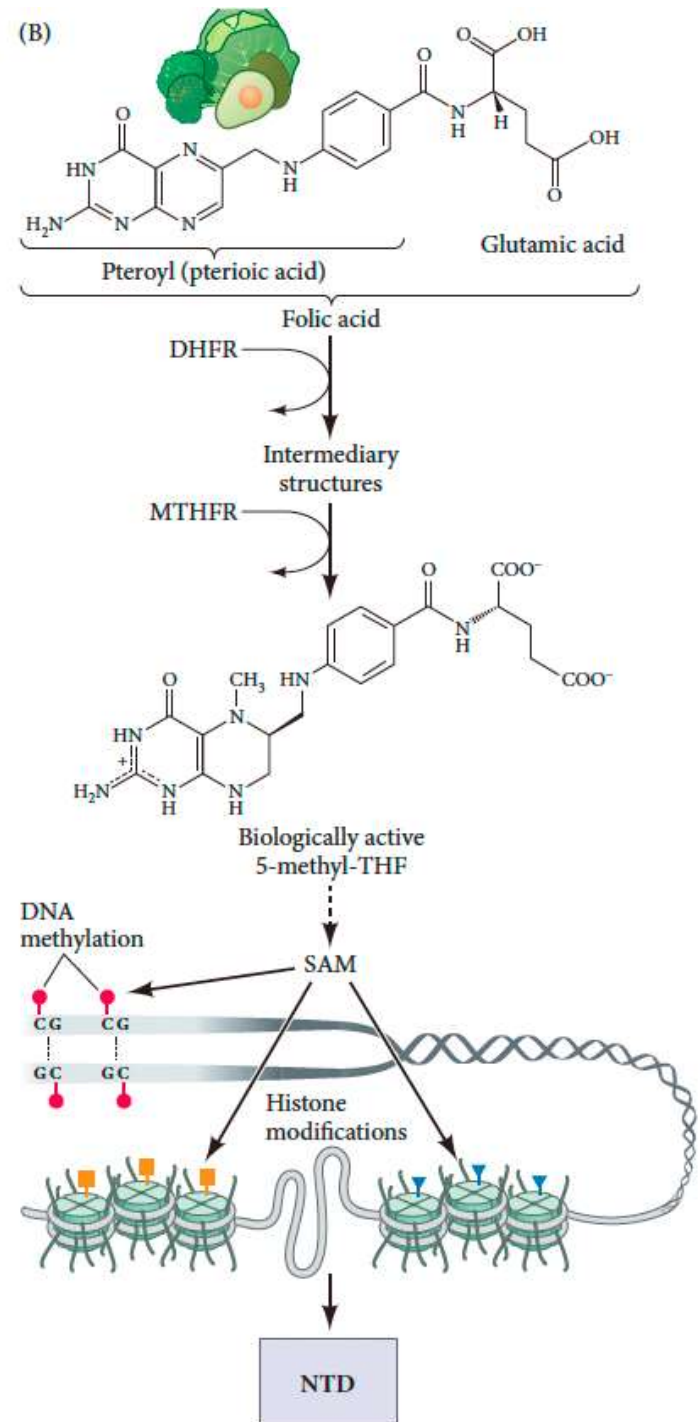


# Environmental influences on neural tube defects and the role of folic acid

(A)



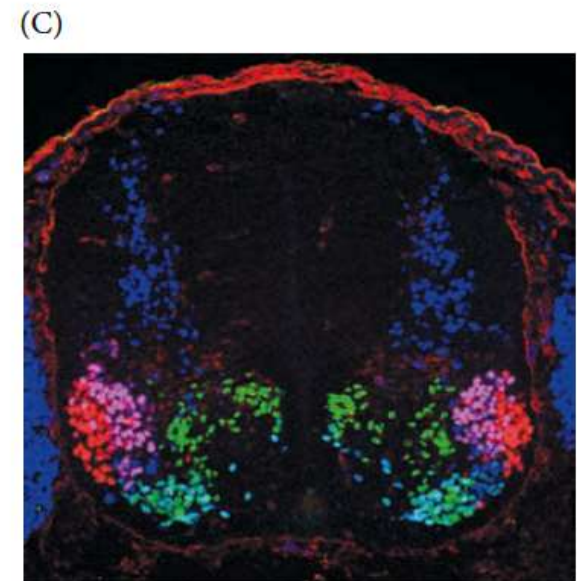
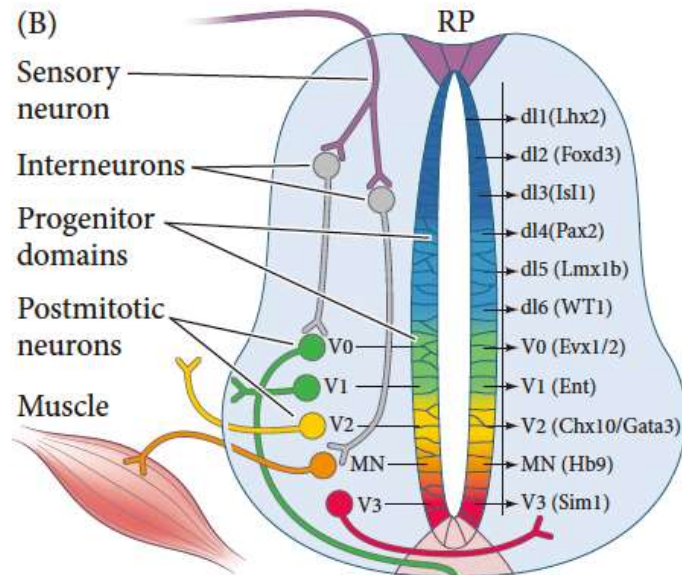
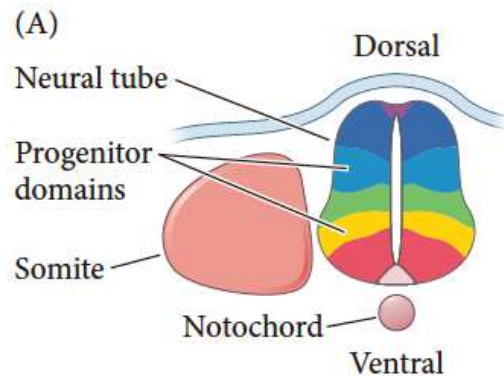
(B)



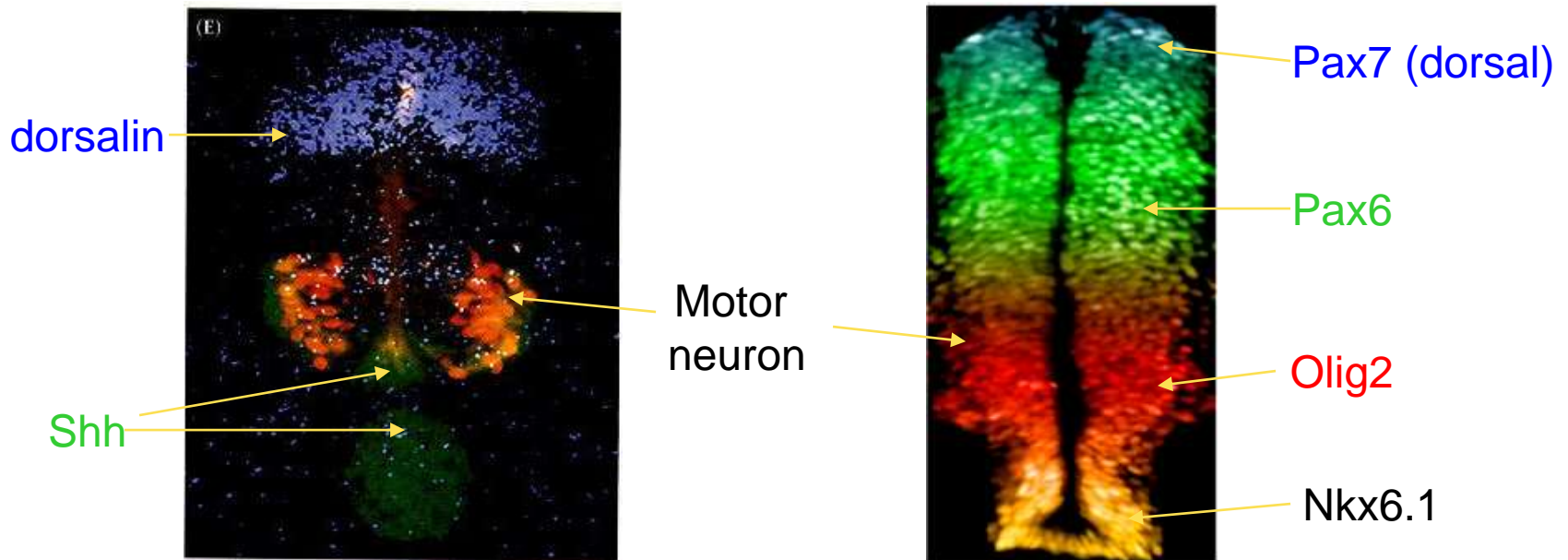
# Patterning of the neural tube



# DV patterning of the spinal cord



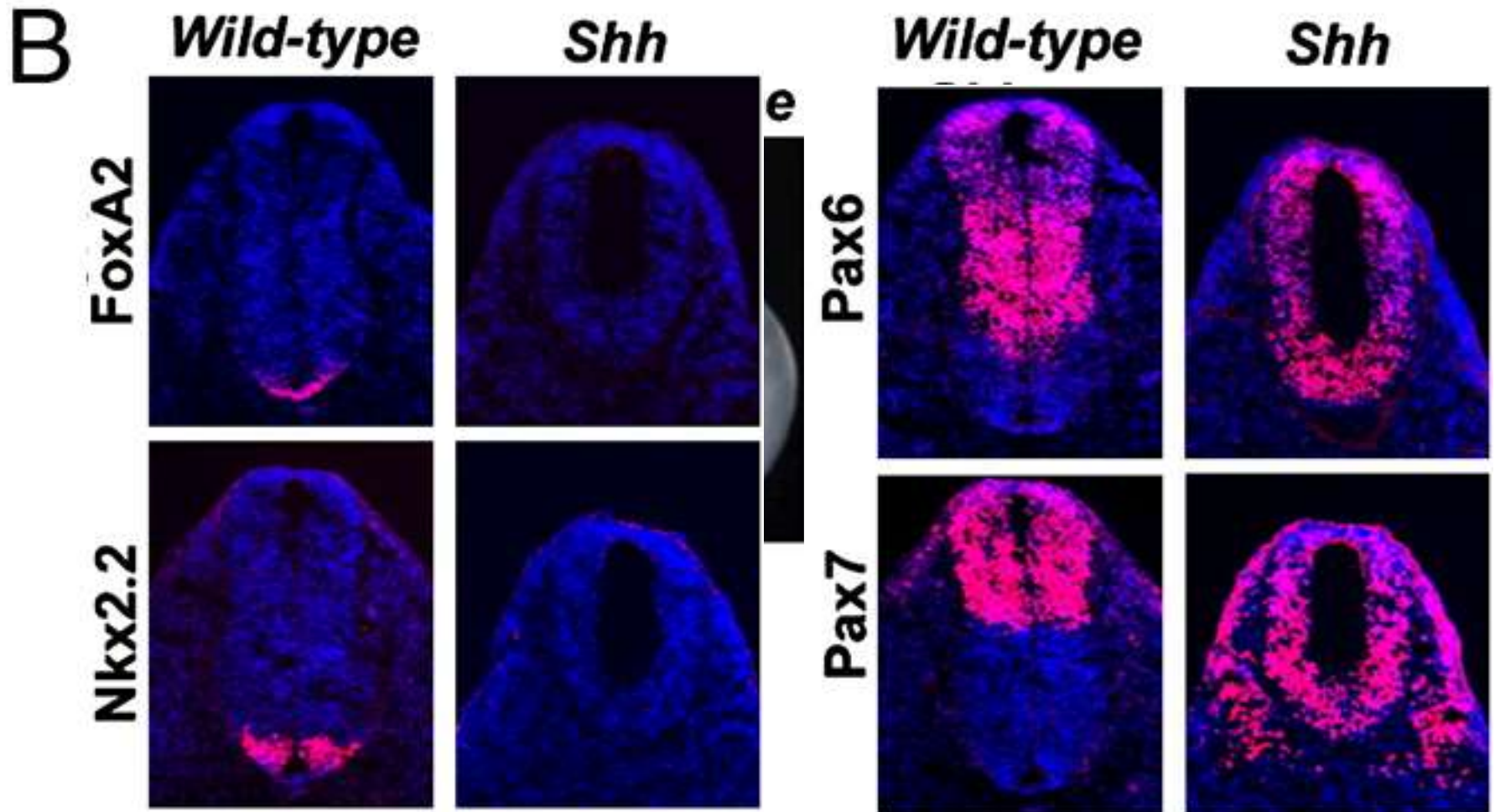
# DV patterning of neural tube in chick



How does DV patterning form in neural tube?

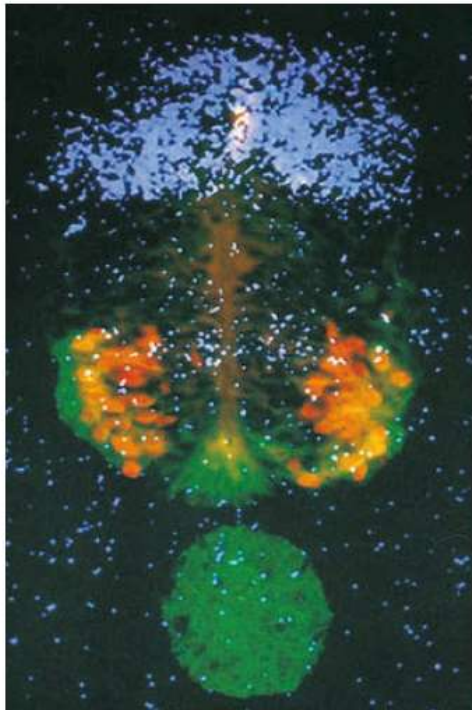


# Shh is required for ventral neural cells

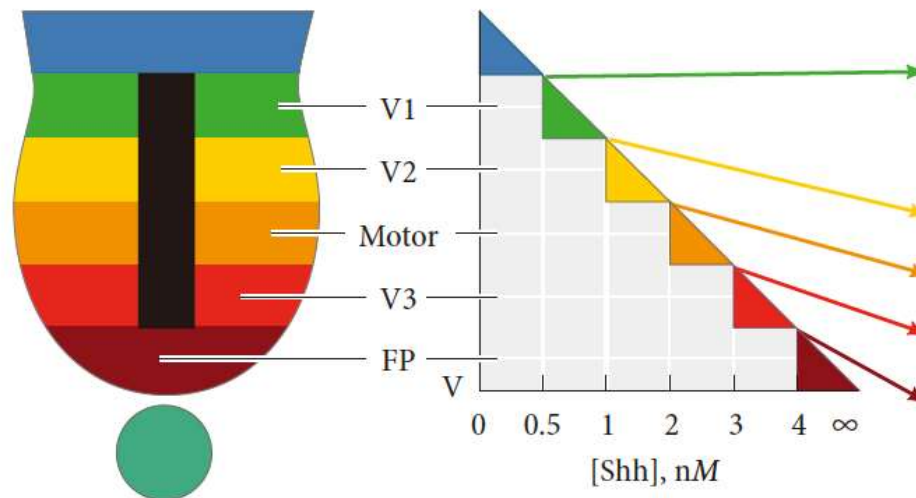


# DV patterning of neural tube is controlled by *shh* & TGF- $\beta$

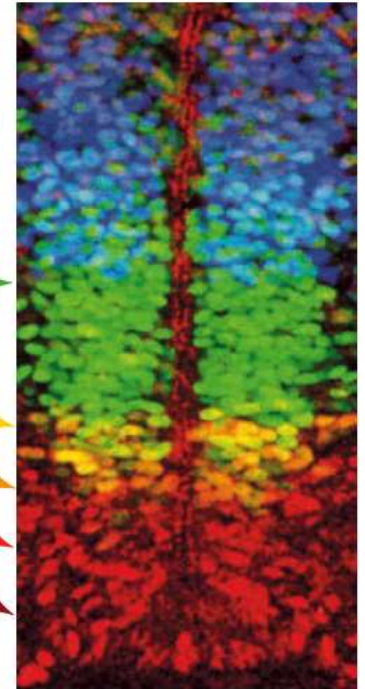
(E)



(F)

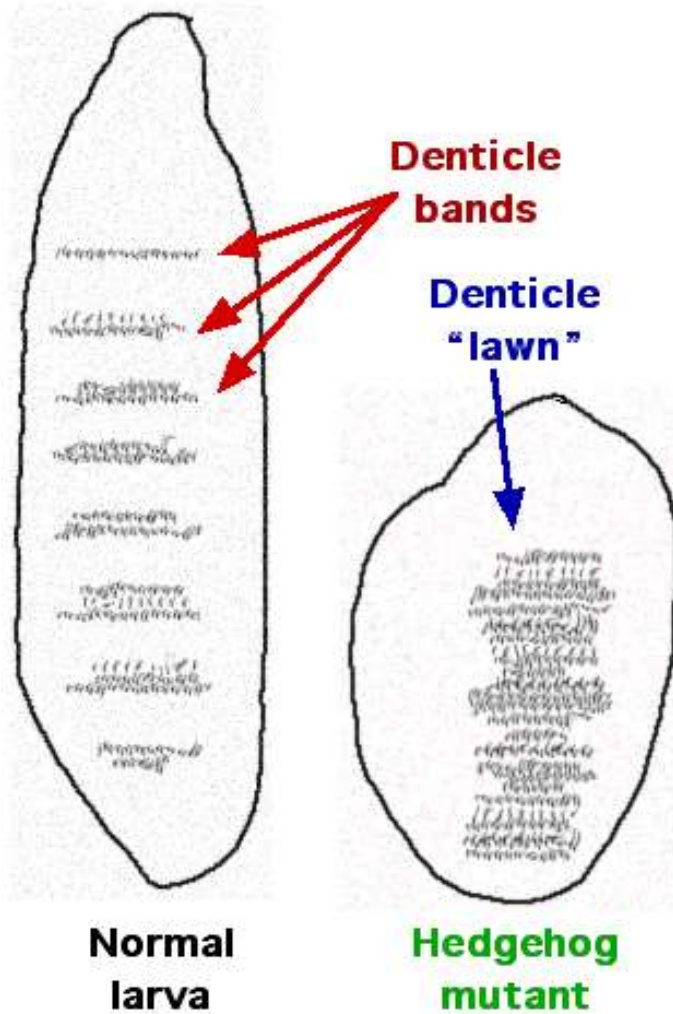


(G)



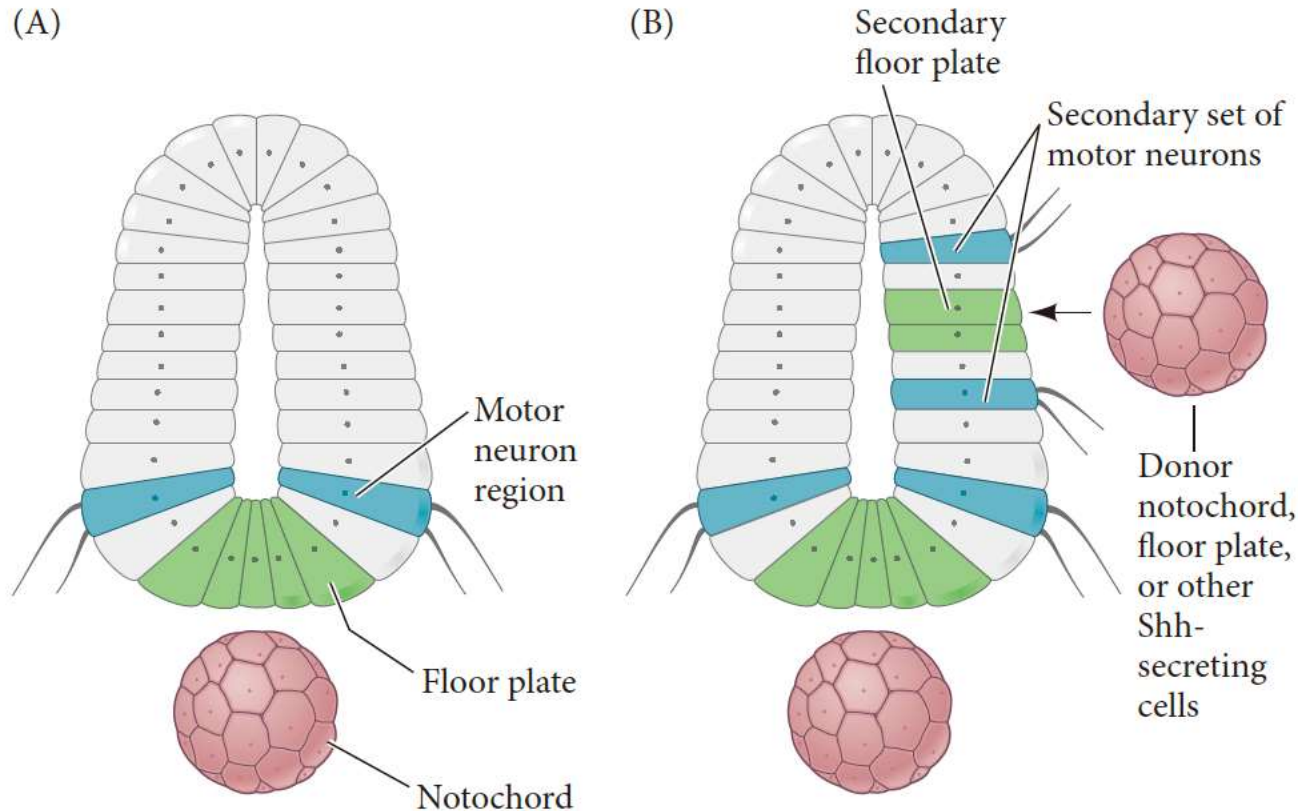
*Pax7* (blue, the dorsal neural tube cells),  
*Pax6* (green), and *Nkx6.1* (red).  
*Nkx6.1* & *Pax6* overlap (yellow), motor neurons

# Shh



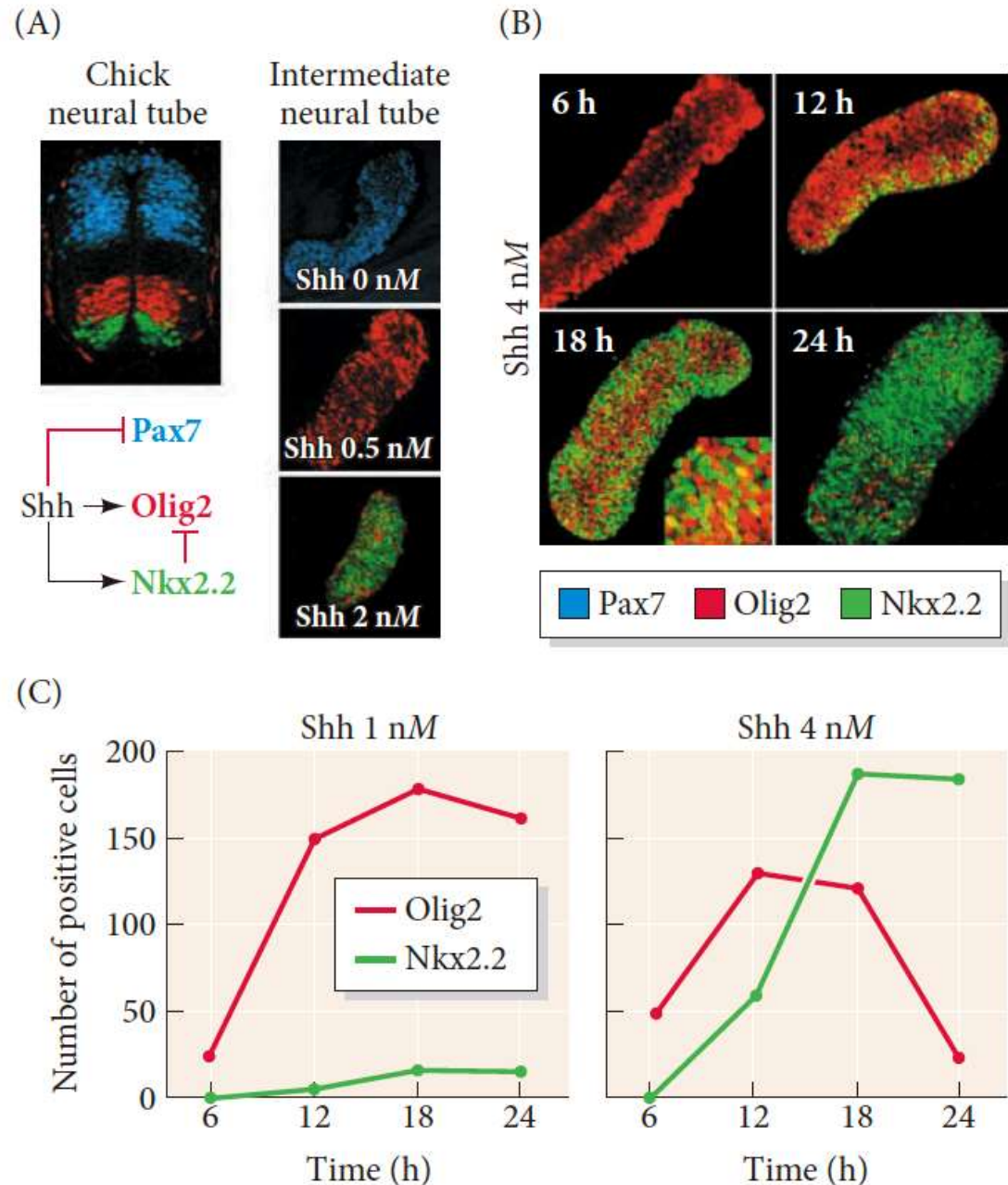
a blue 15-year old  
anthropomorphic hedgehog  
run at supersonic speeds  
curl into a ball primarily to attack  
enemies

# Notochord-derived Shh induces ventral neural tube structures

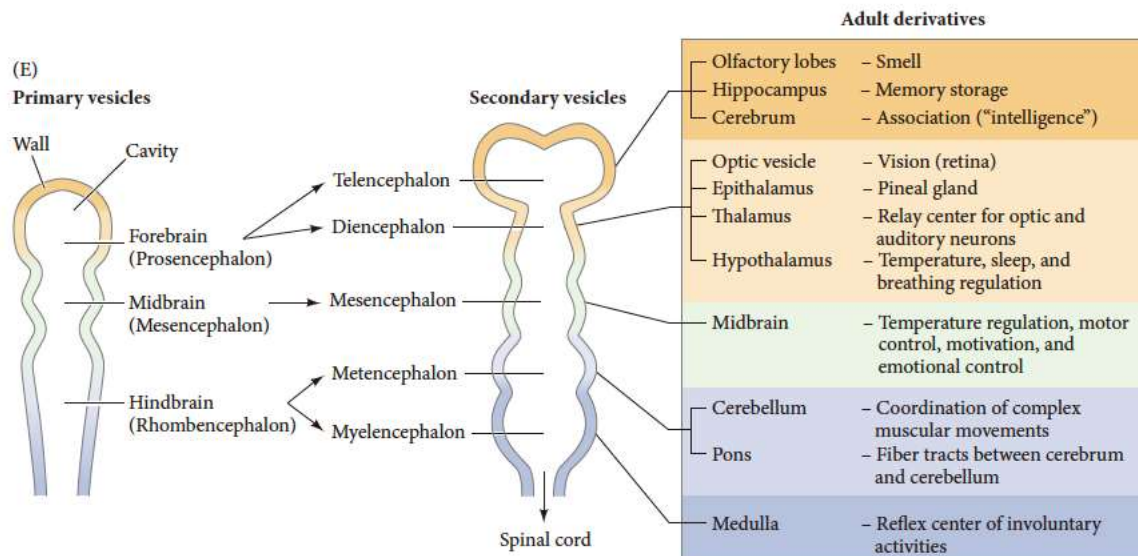
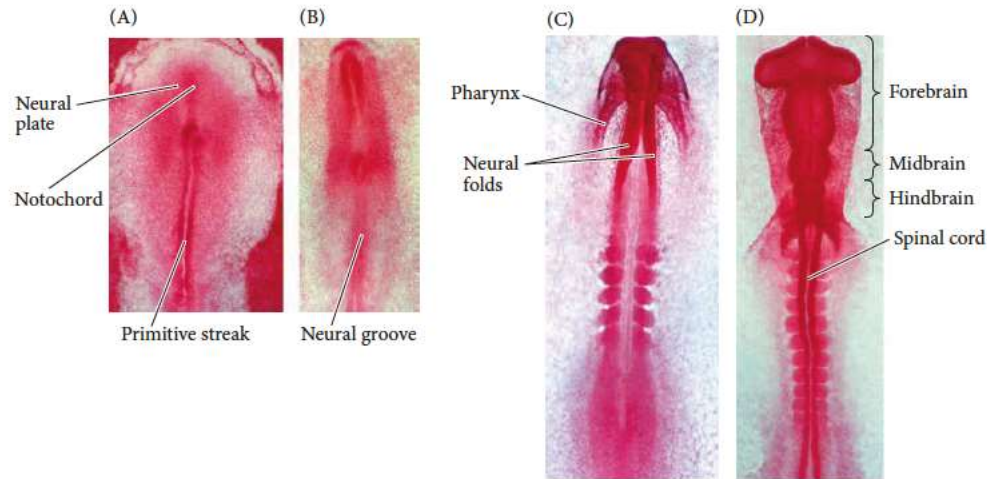




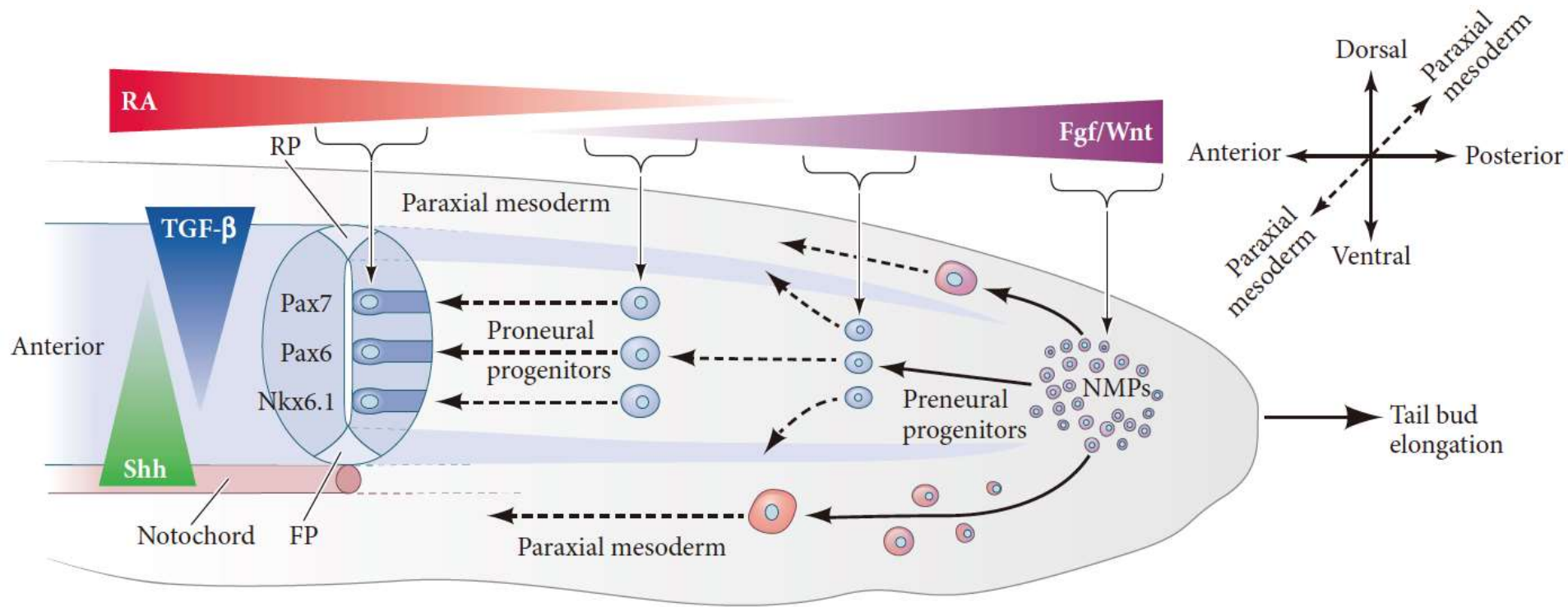
# Neural tube gene expression responds to both concentration and duration of Shh



# Neural tube differentiation: anterior-posterior patterning



# Model for maturation and specification of the caudal region of the spinal cord.

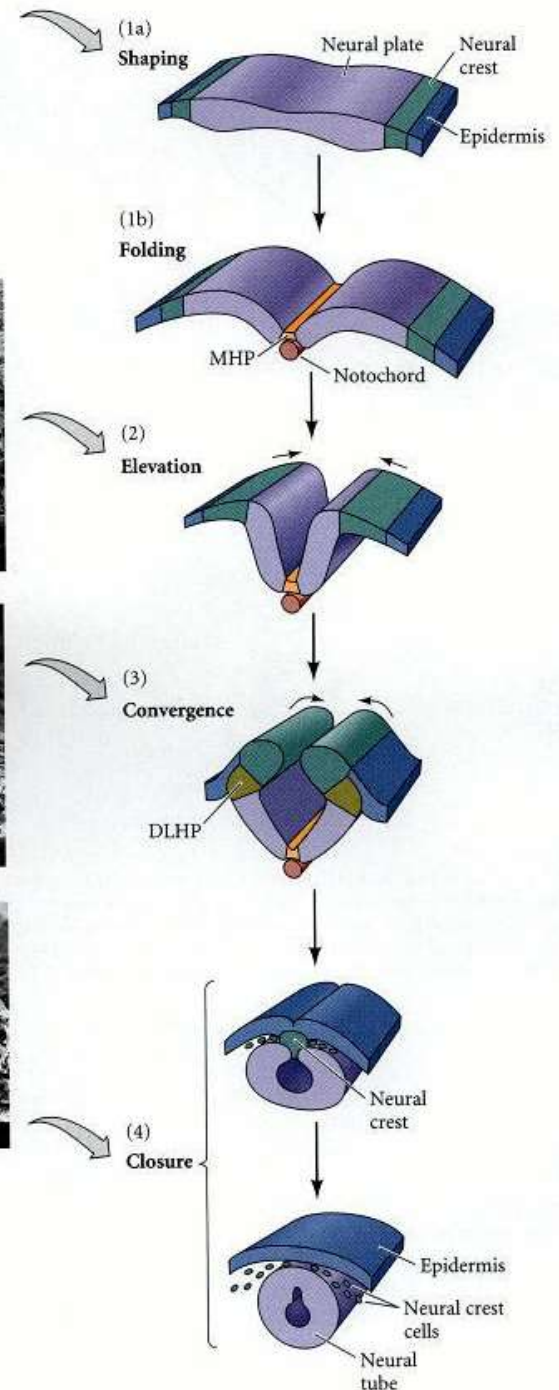
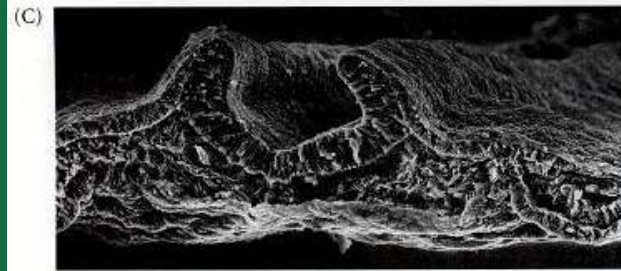


# Summary (I)

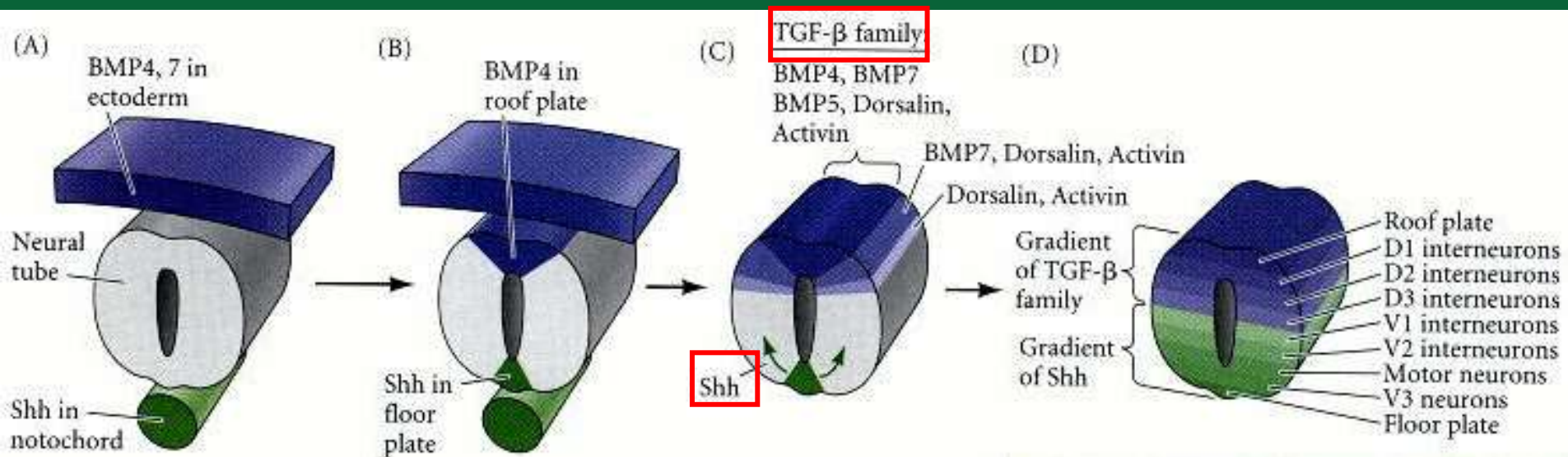
- Key word:  
primary & secondary neurulation, Shh
- Event and mechanism  
neural tube formation, neural tube  
patterning (DV patterning)



# Graph Summary (I)



# Graph Summary (II)



# outline

- Ectoderm

- 1) neural tube formation and differentiation

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- 3) eye development

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- Endoderm

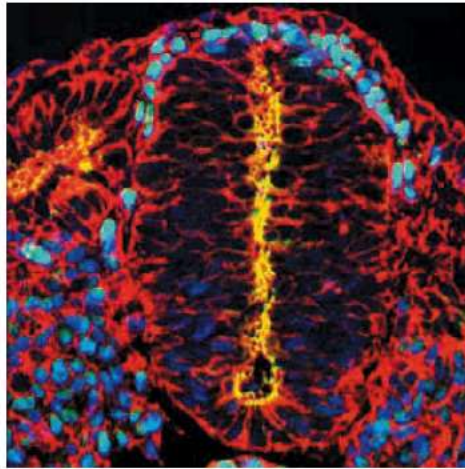
- gut

# Neural crest cells (神经嵴细胞)

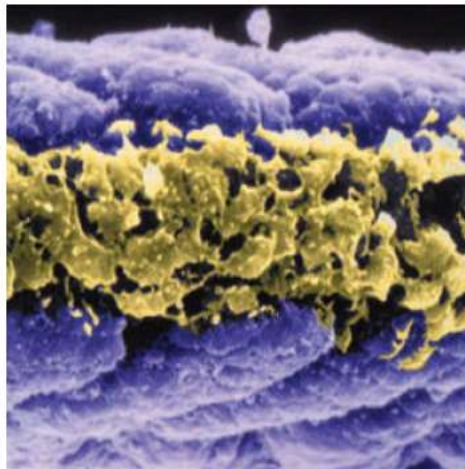
- Specification: at the neural plate-epidermis boundary.
- Feature:
- Migration.
- Multipotency: can differentiate into different type of cells depending on the location.

# Neural crest cell formation

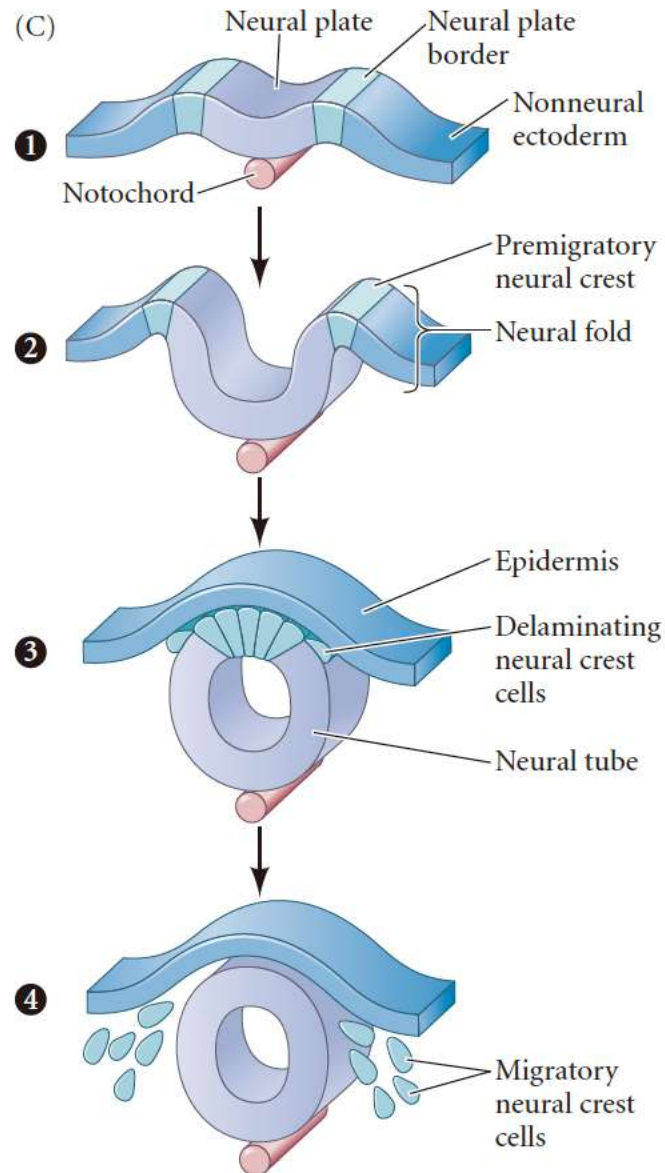
(A)



(B)

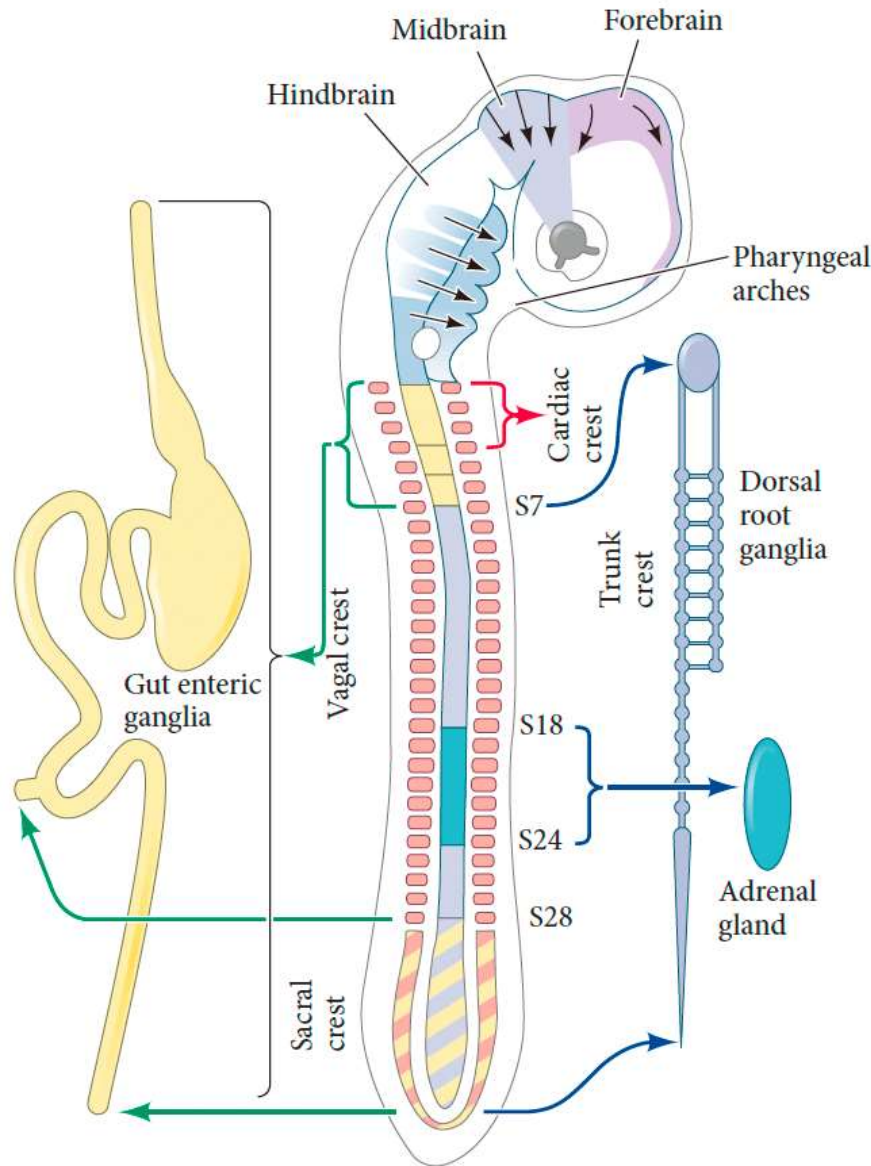


(C)



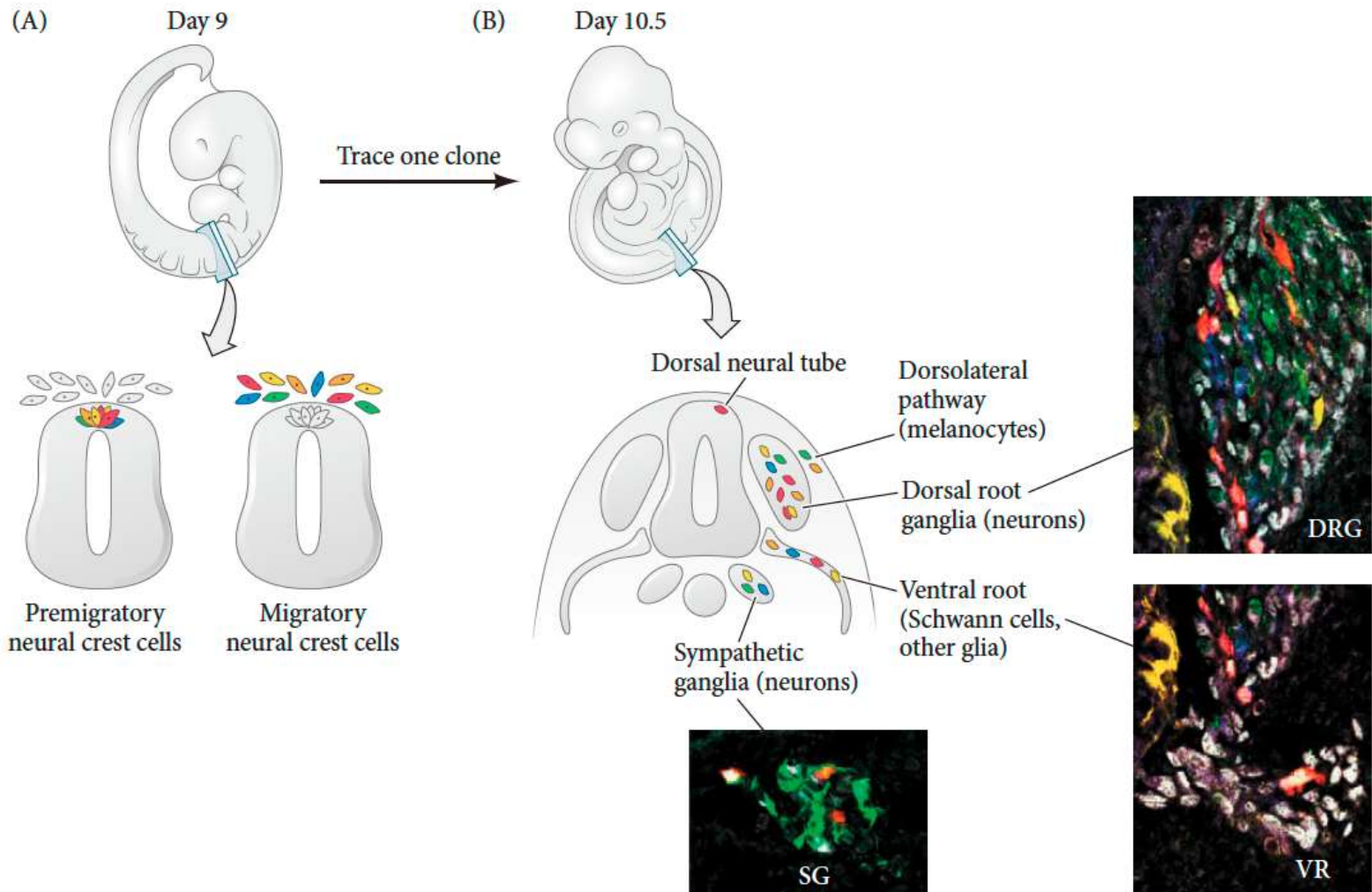


# Regions of neural crest

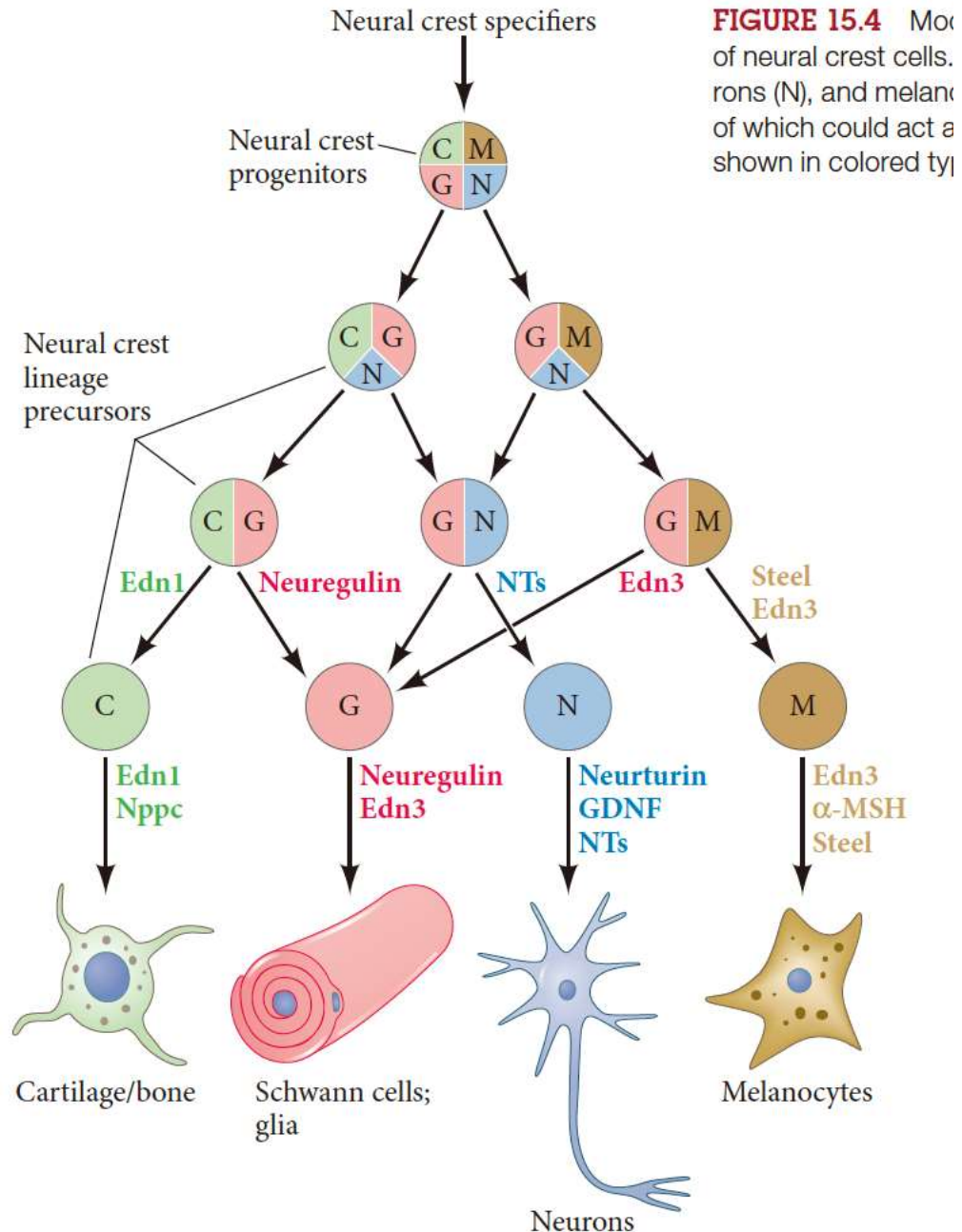


1. **cranial (面部) neural crest:** → cranial cartilage (面部软骨), bone, neurons, glia, etc;
2. **trunk (躯干) neural crest:** → dorsal root ganglia (背部神经节), melanocytes (色素);
3. **vagal (迷走神经) and sacral (骶骨) neural crest:** → parasympathetic ganglia (副交感神经) of the gut
4. **cardiac (心) neural crest:** subregion of the vagal neural crest (交感神经脊的一部分), → melanocytes, neurons, cartilage, connective tissue (结缔组织)

# Trunk neural crest cells are multipotent stem cells



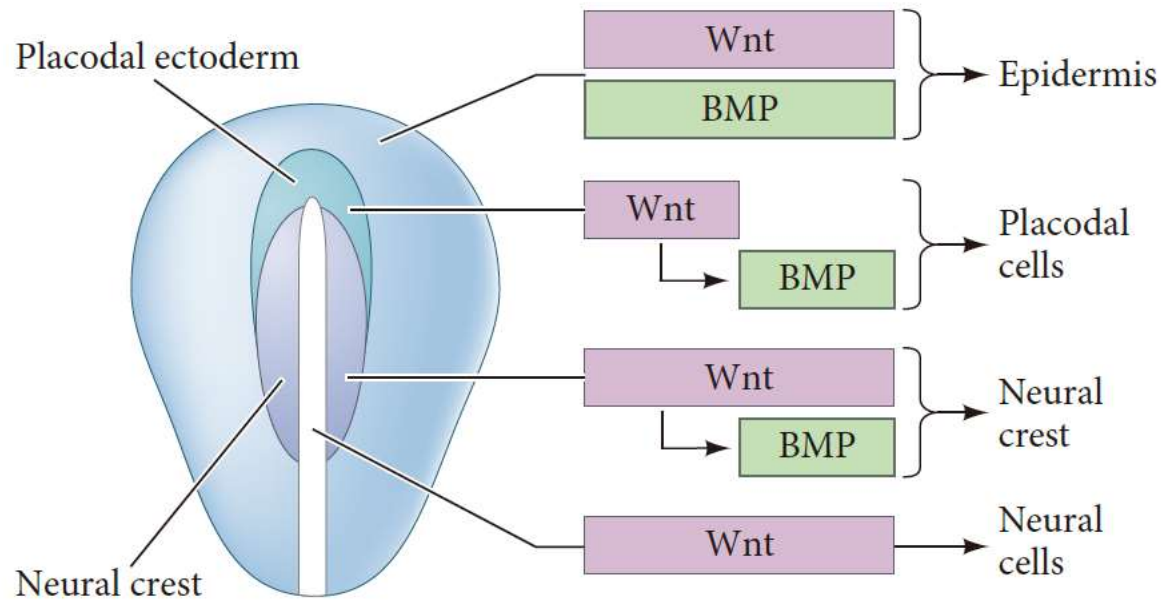
# Model for neural crest lineage segregation and the heterogeneity of neural crest cells.

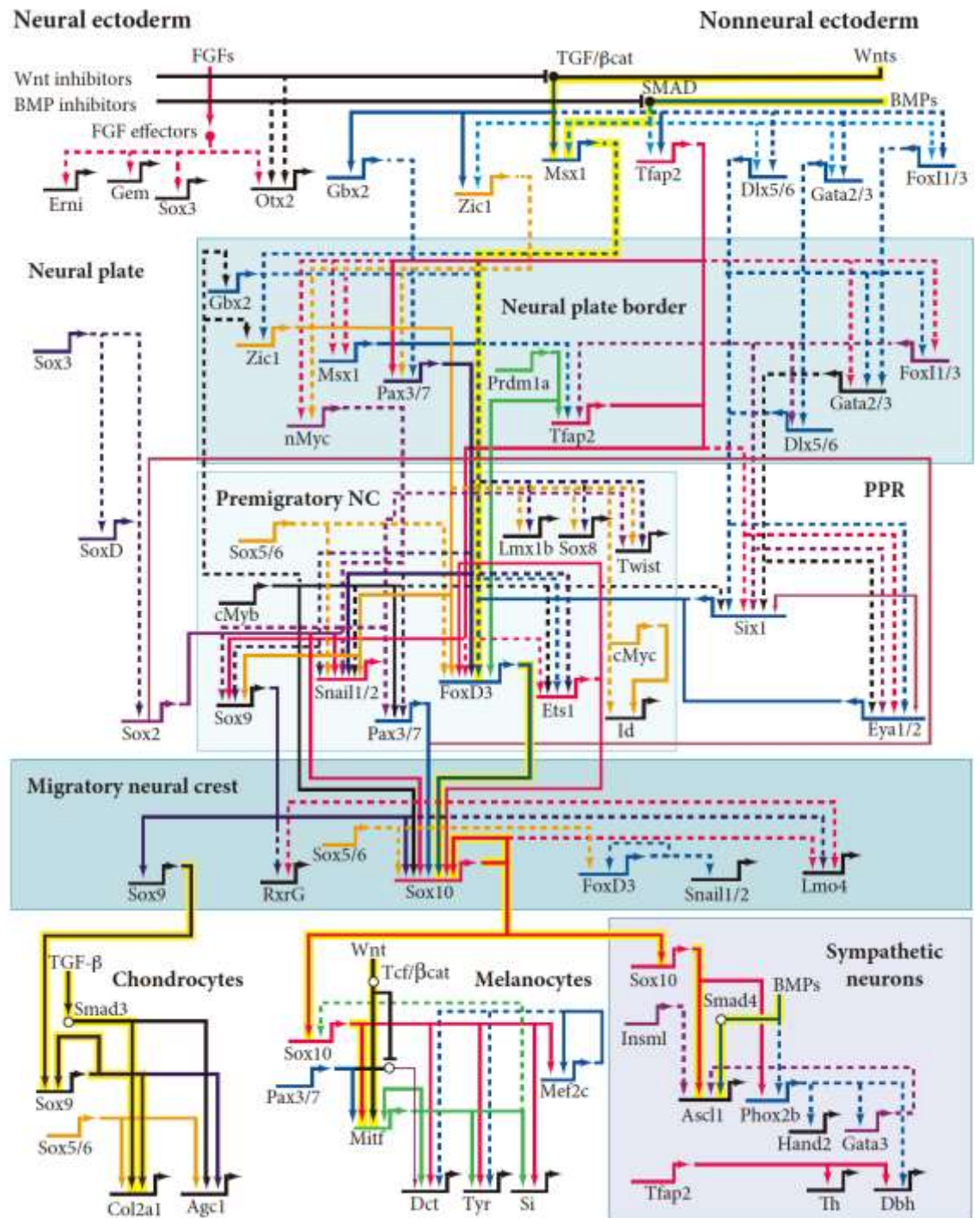


**FIGURE 15.4** Model of neural crest cell lineages (N), and melanocytes (M), and of which could act as shown in colored type



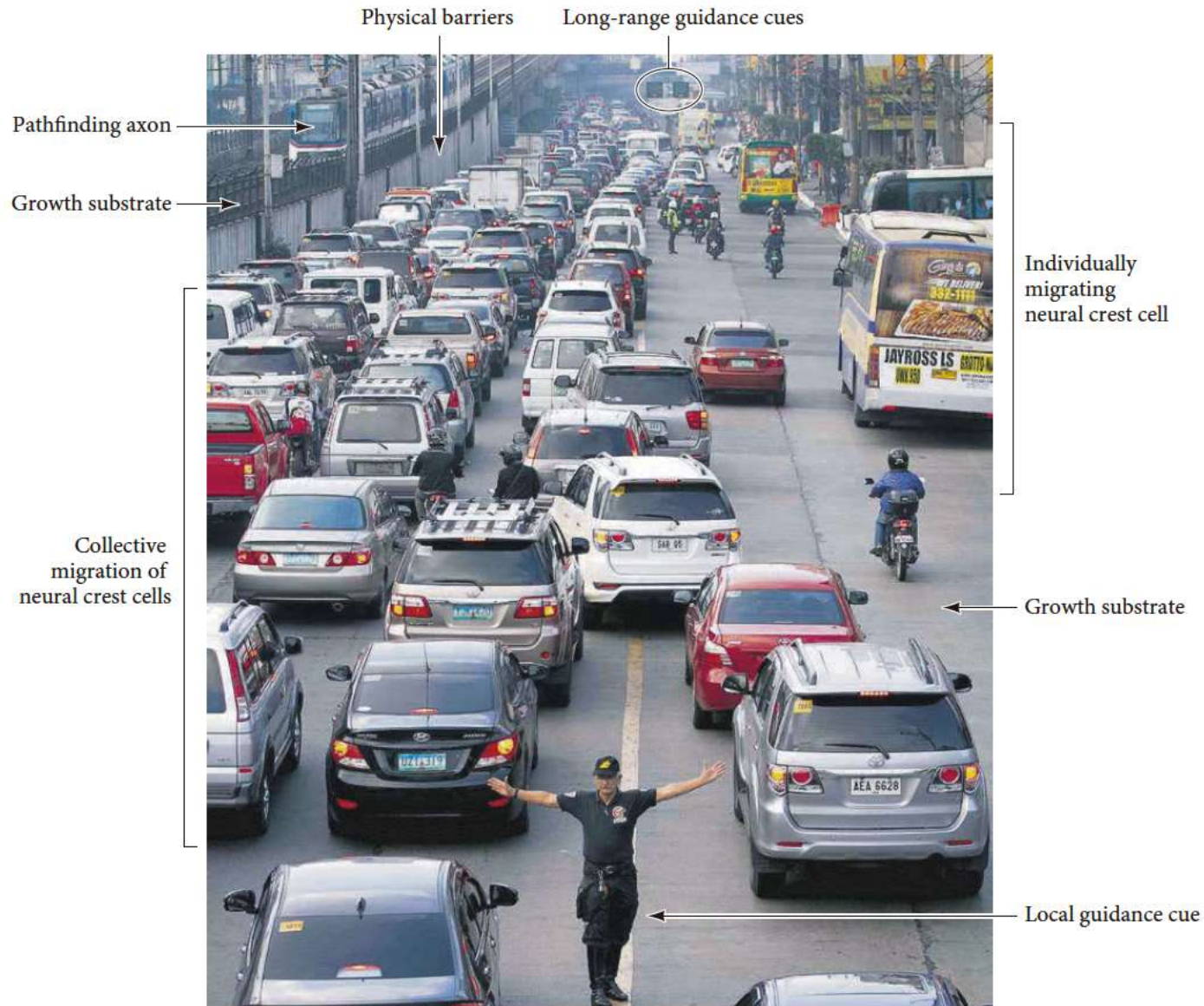
# Specification of neural crest cells



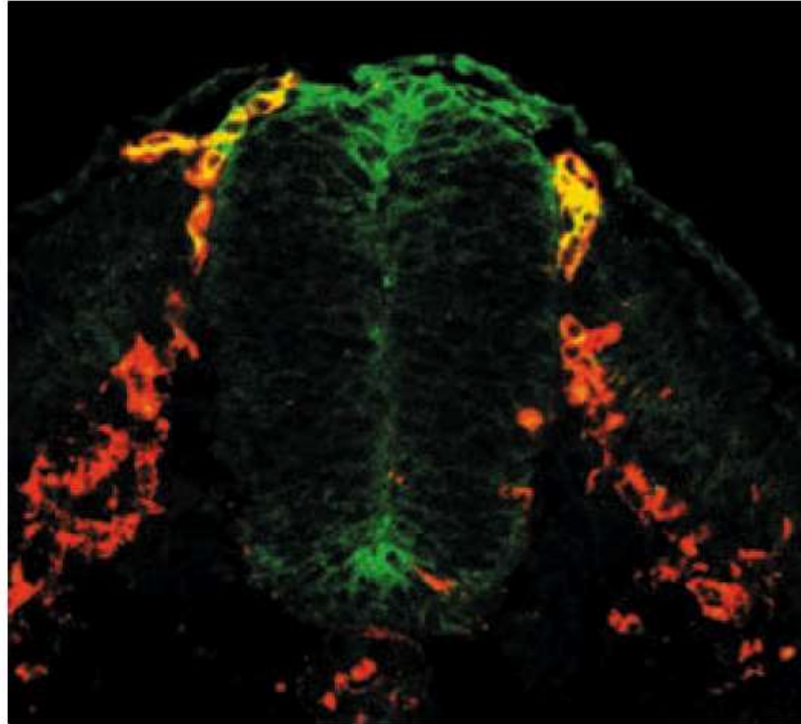


# Neural Crest Cell Migration

# Analogy of neural crest to the guidance and movement



# Delamination of neural crest cells

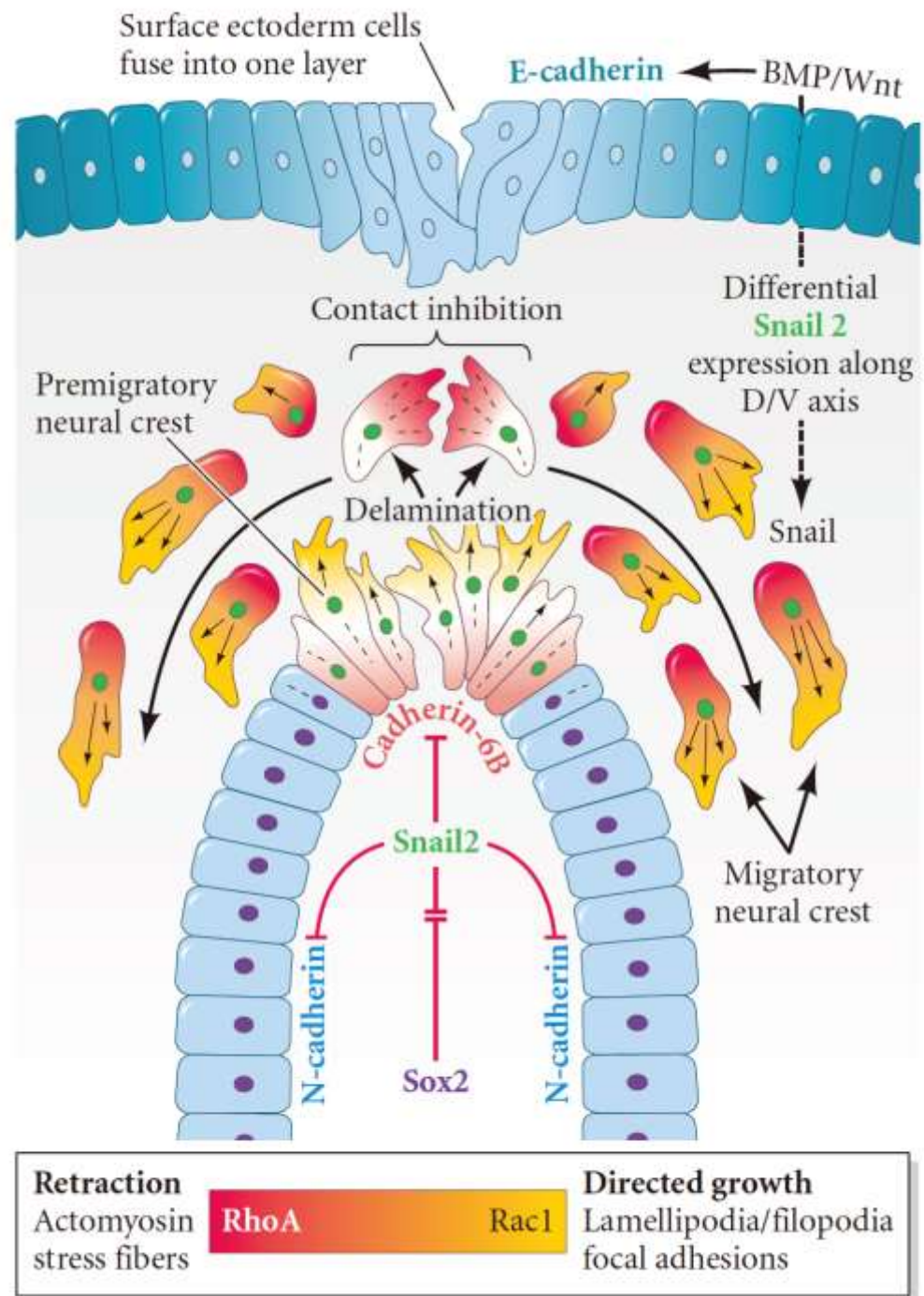


RhoB protein (green) is expressed in cells as they delaminate.

Neural crest cells lose their adhesive junctions and separate from the epithelium in a process known as **delamination**.

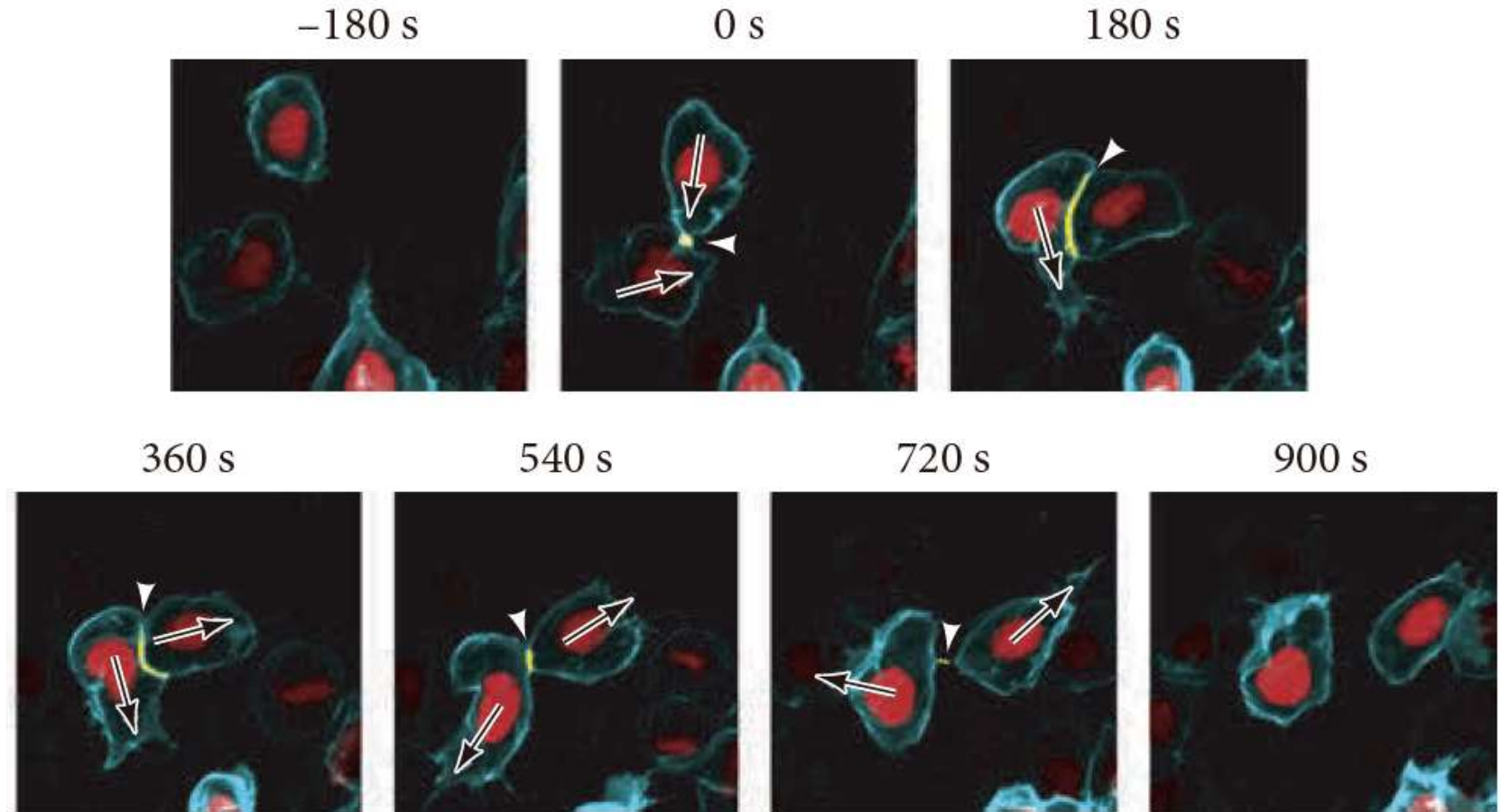


# Neural crest delamination and migration by contact inhibition

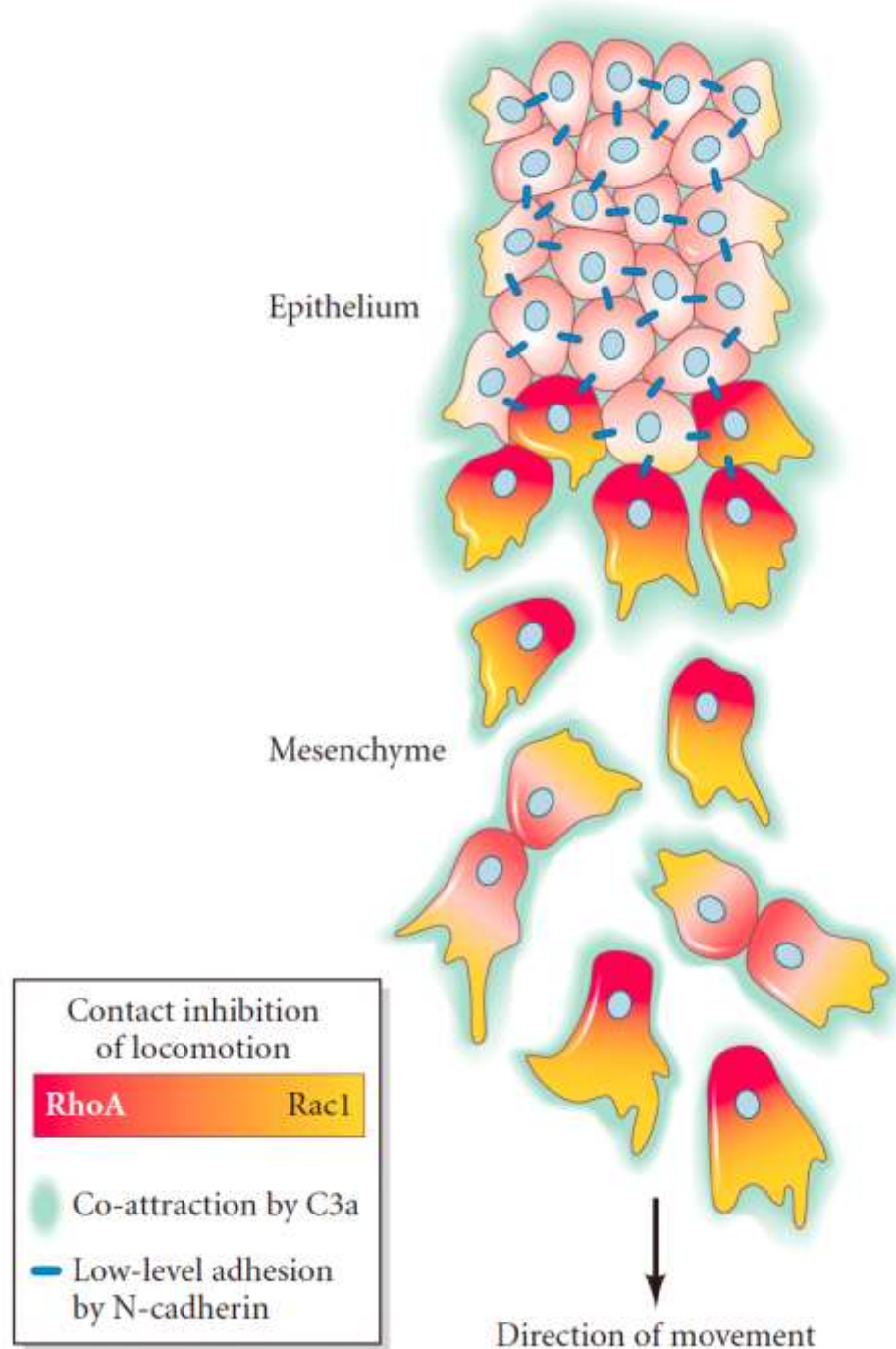




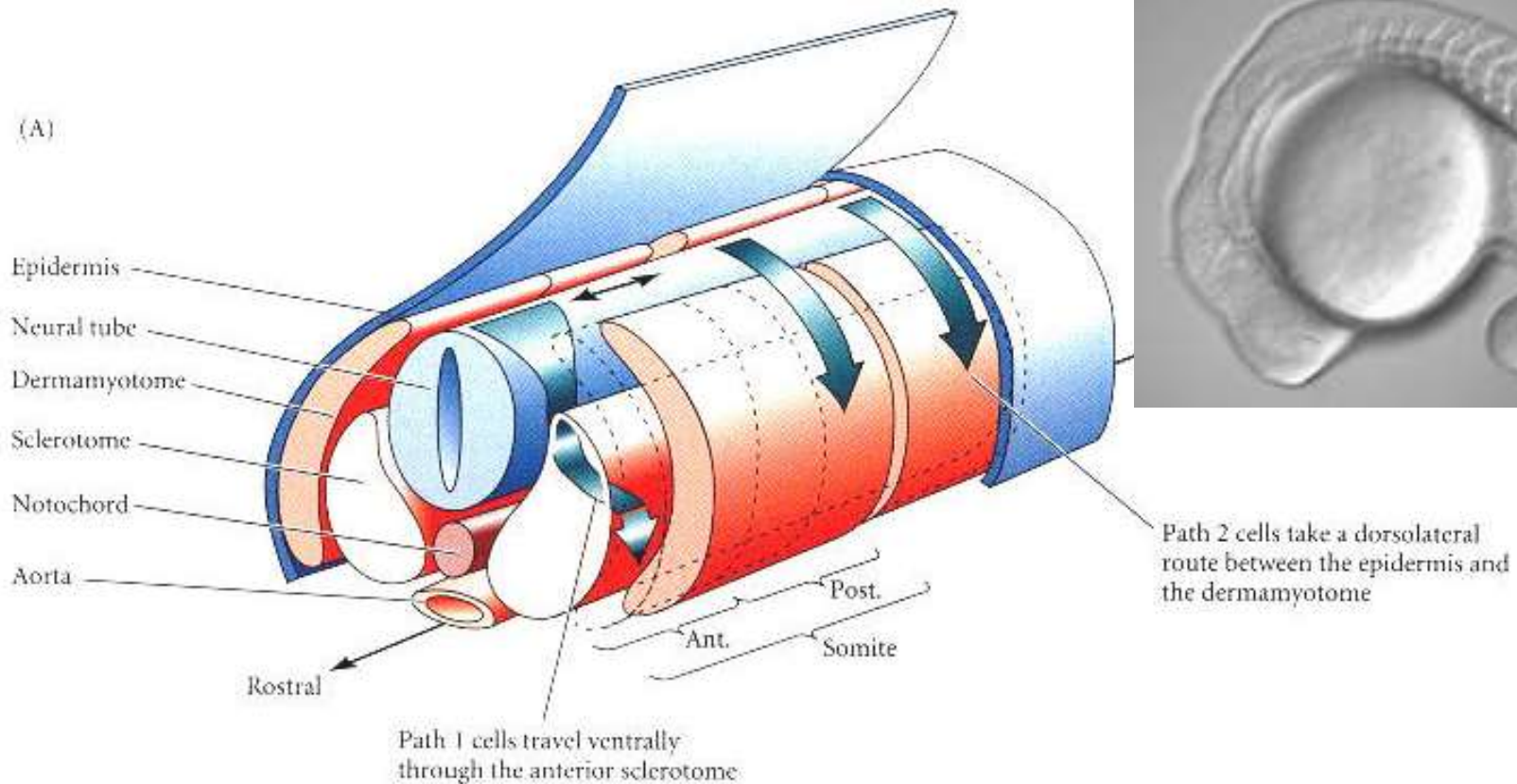
# Migrating neural crest cells demonstrate contact inhibition of locomotion in a live zebrafish embryo



# Model of collective migration of neural crest cells



# neural crest cell Migration in trunk of the chick embryo



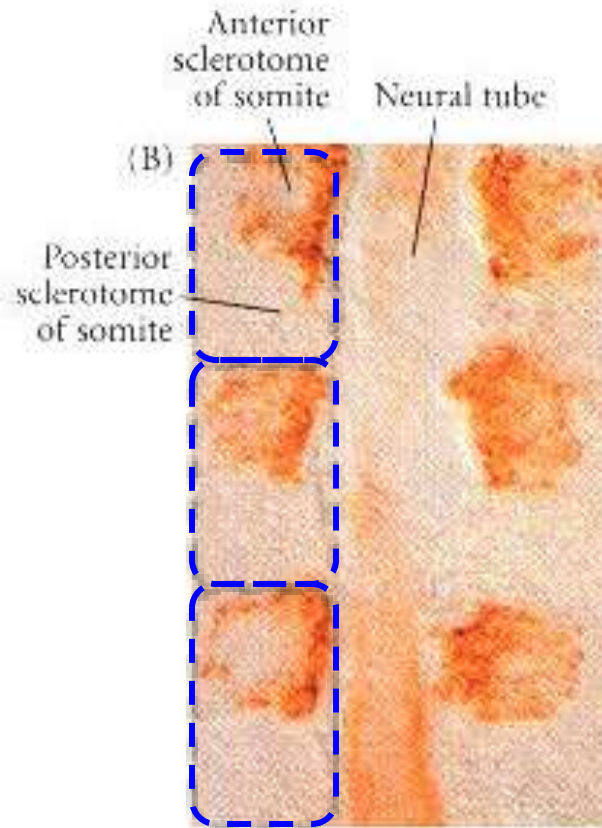
Two major migratory pathways:

**The ventral pathway:** travel through anterior part of the sclerotome (生骨节).

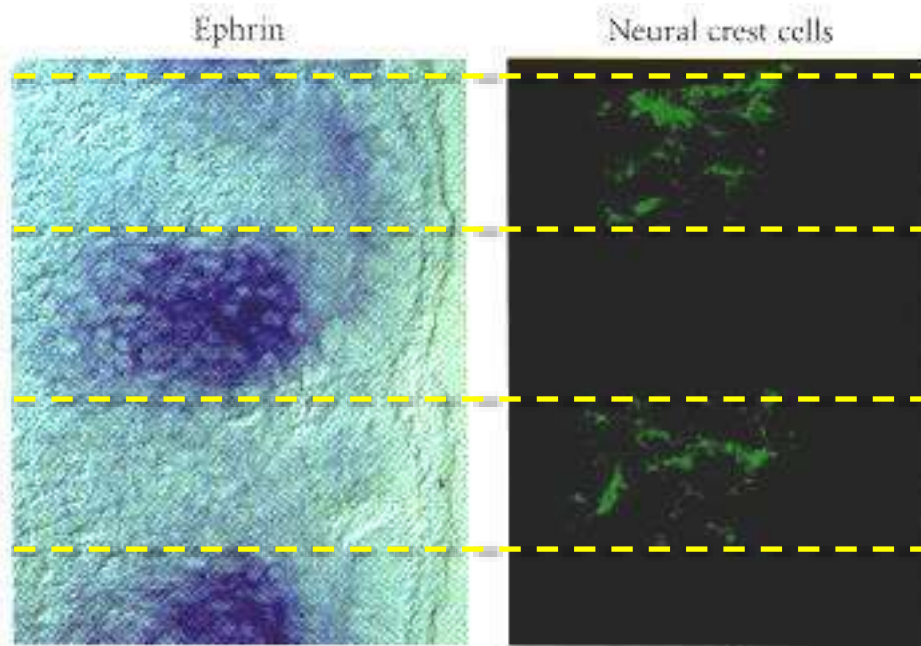
→ sympathetic and parasympathetic ganglia, dorsal root ganglia.

**The dorsolateral pathway:** travel along the dorsolateral region between epidermis and dermamyotome (生肌节). → melanocytes.

# Neural crest cells only migrate through anterior part of the somite



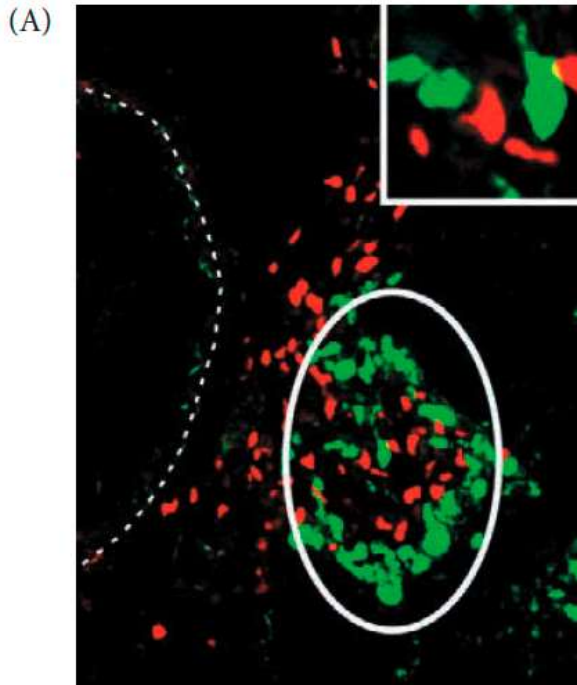
# Segmental restriction of neurons by ephrin proteins



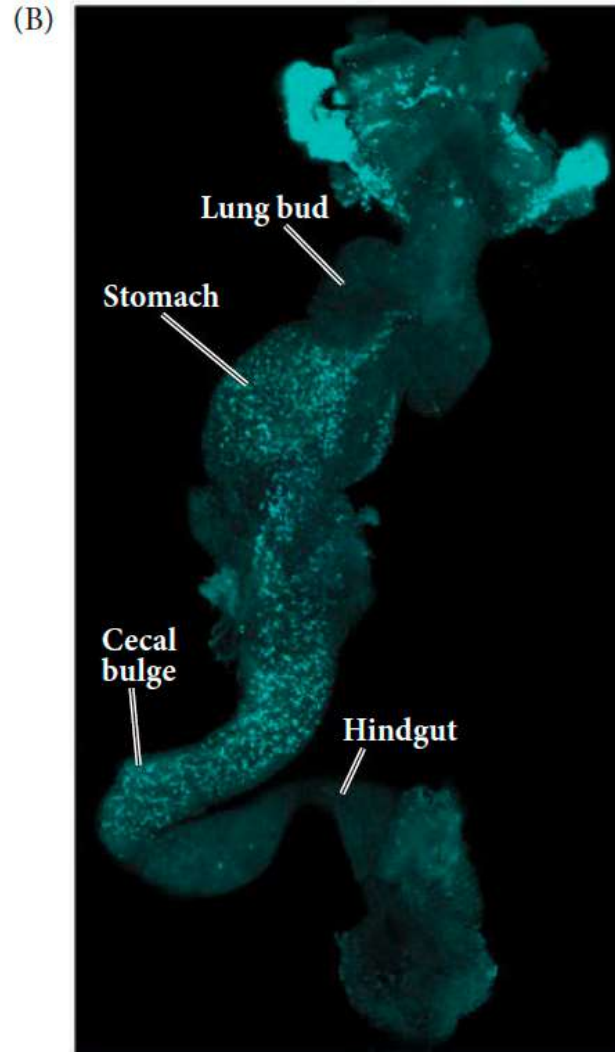
(A)



# cell differentiation in the ventral pathway



**Sox8**: neural crest cells  
**SF1**: the adrenal cortical  
cells



the enteric (gut) ganglia for peristalsis



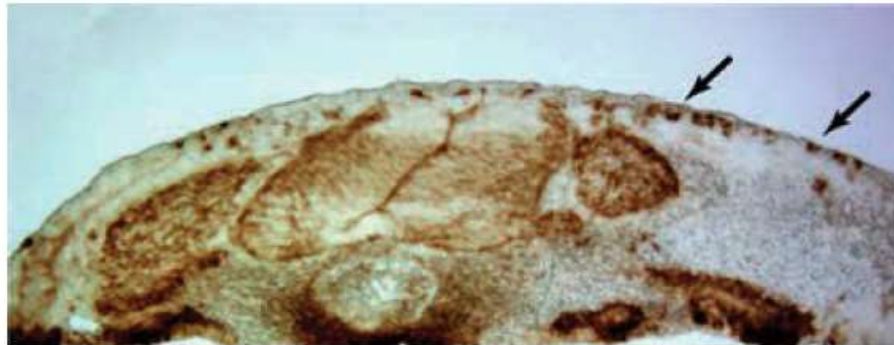
# Neural crest cell migration in the dorsolateral pathway through the skin

(A)



ISH of  
mouse @ e11

(B)



Stage 18  
chick embryo

# Variable melanoblast migration, caused by different mutations

(A)



*Mitf*<sup>+/-</sup>

(B)



*endothelin receptor B*<sup>+/-</sup>

(C)



(D)

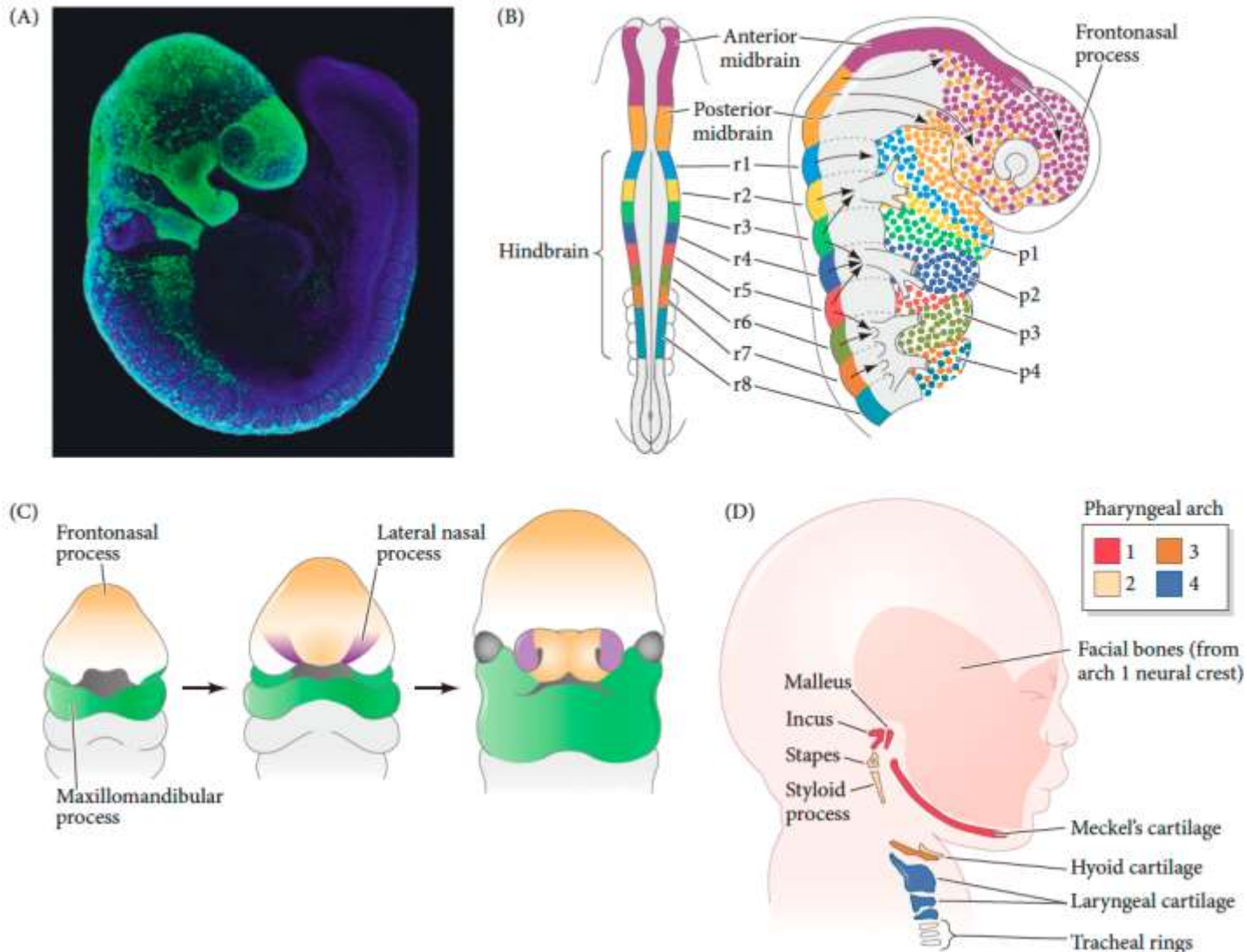


*Kit*<sup>-/-</sup>

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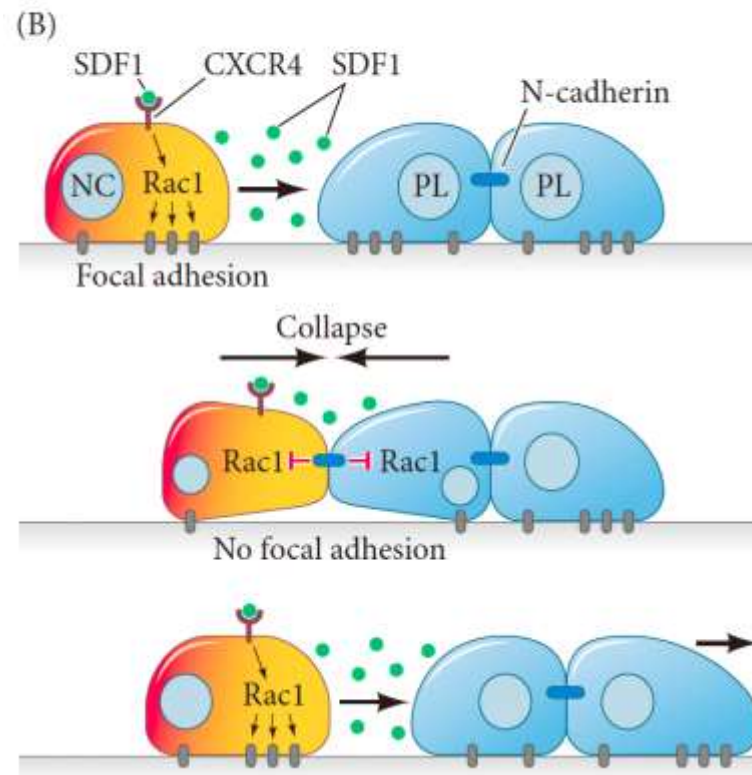
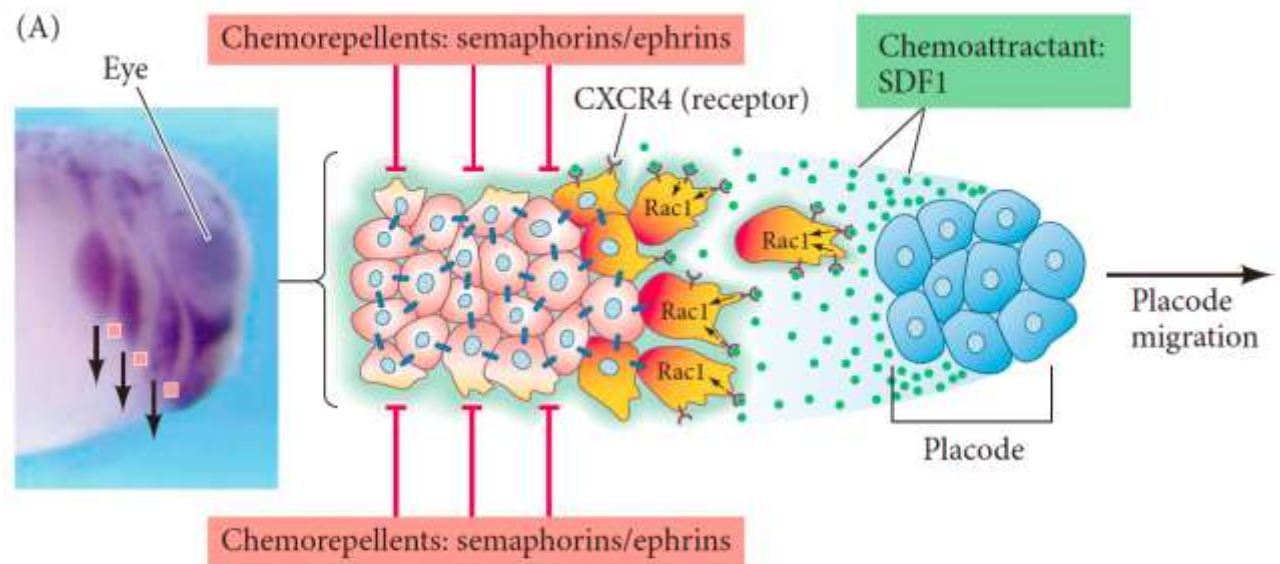
Spotted pigmentation & deafness:  
the random death of melanoblasts

# Cranial neural crest cell migration in the mammalian head





# "Chase and run" model for chemotactic cell migration



## Summary (II)

- Key word:  
neural crest cells, multipotency
- Event and mechanism:  
neural crest cells formation, migration

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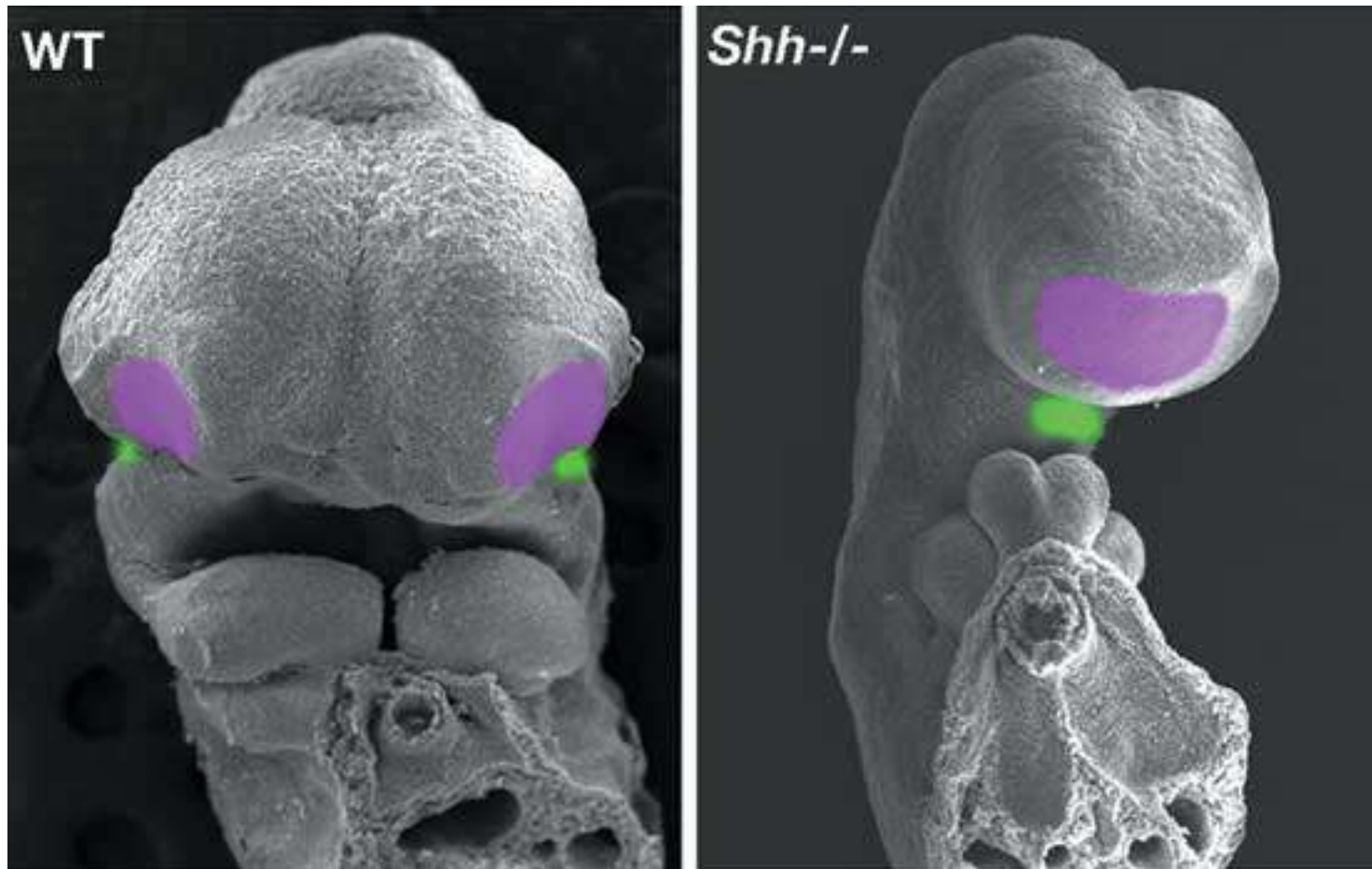
- gut

# Cyclolamb and cyclopamine

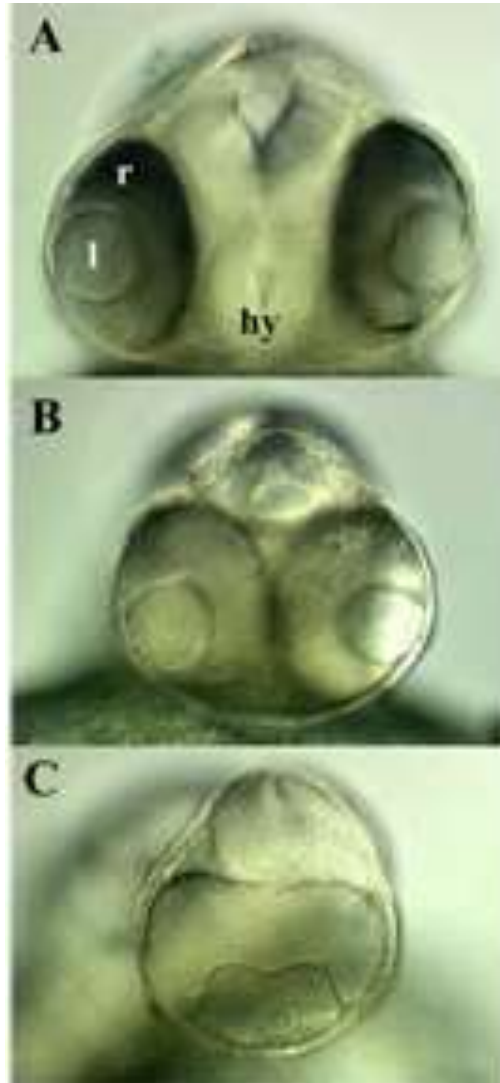


Corn lily (玉米百合)

# Mouse cyclopic mutant



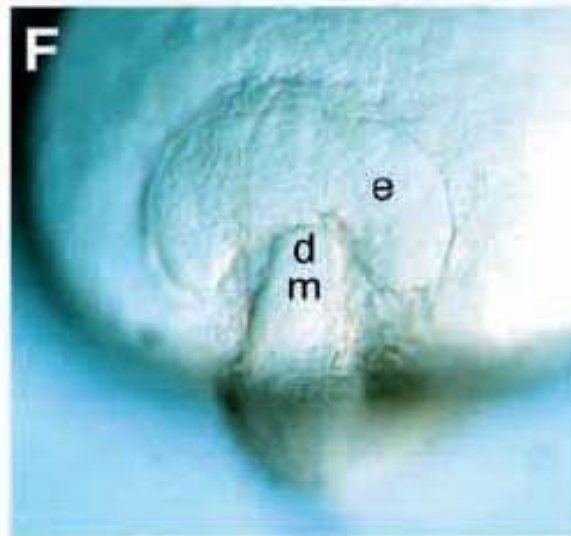
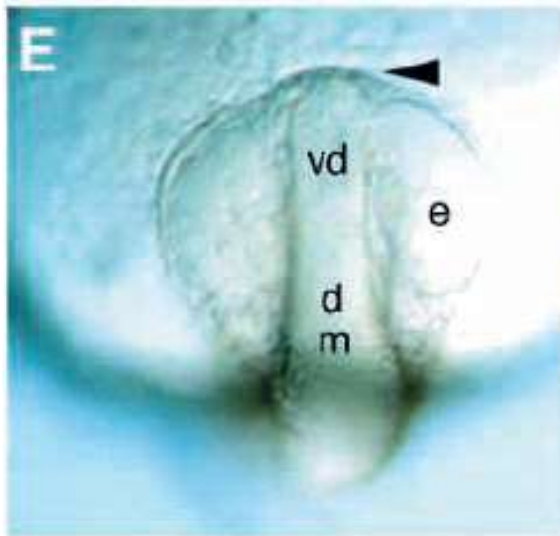
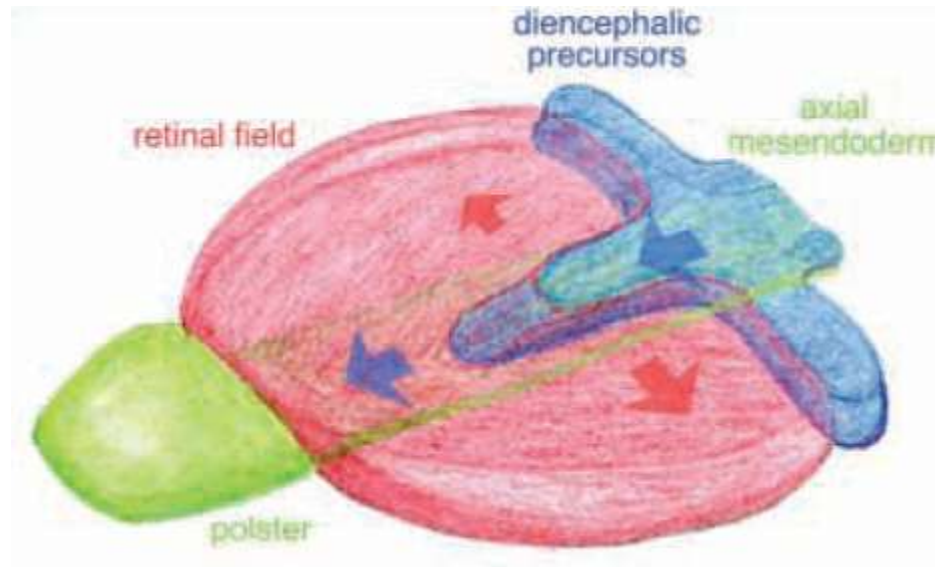
# Zebrafish cyclopic mutant



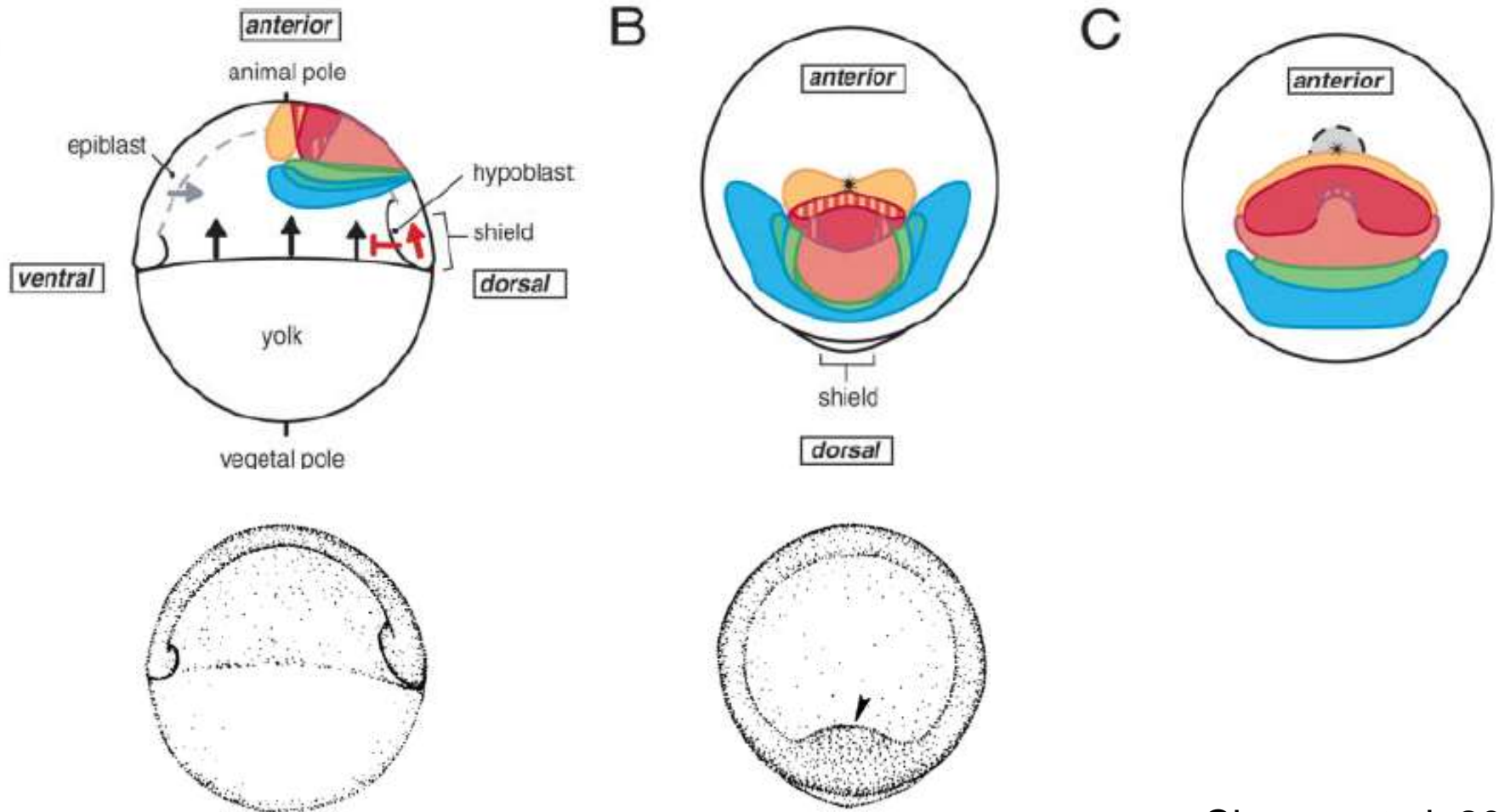
WT

Nodal mutant  
(i.e., cyc, sqt, oep)

# Seperation of the eye field in zebrafish

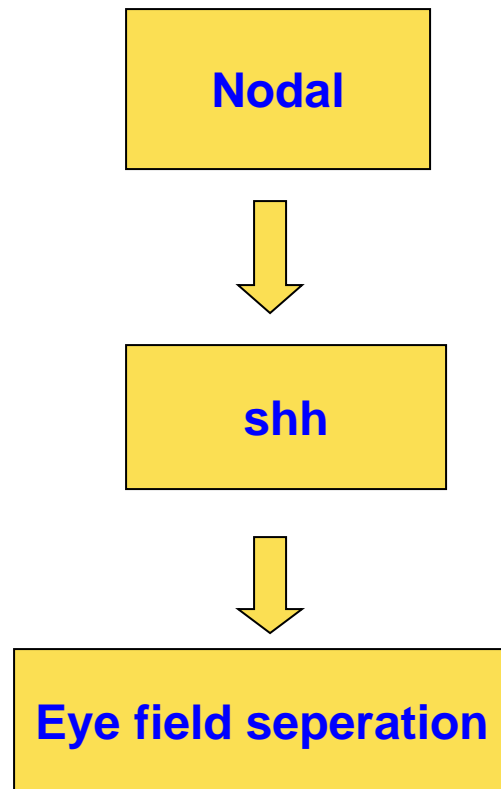


# Seperation of the eye field in zebrafish



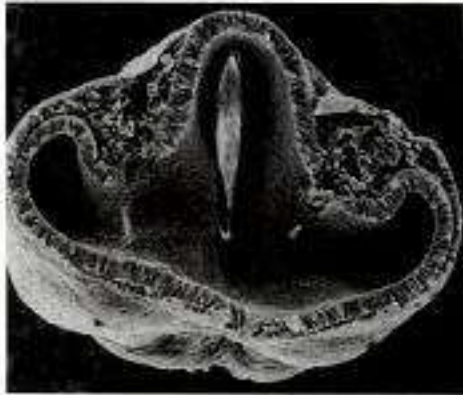


# Seperation of eye field requires Shh and Nodal signal

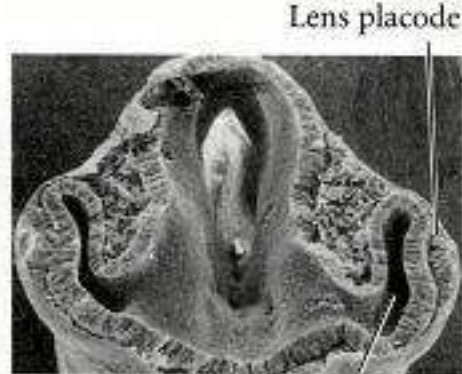


# Development of vertebrate eye

(A) 4-mm embryo



(B) 4.5-mm embryo



Lens placode

Optic vesicle

(C) 5-mm embryo



Lens vesicle

Optic cup

(D) 7-mm embryo

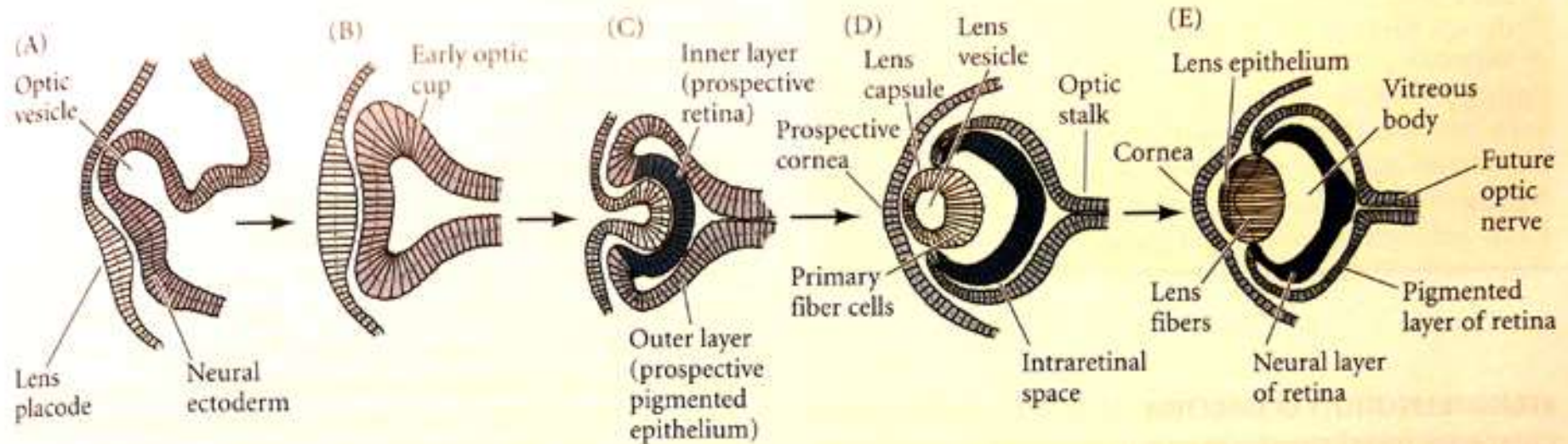


Retina

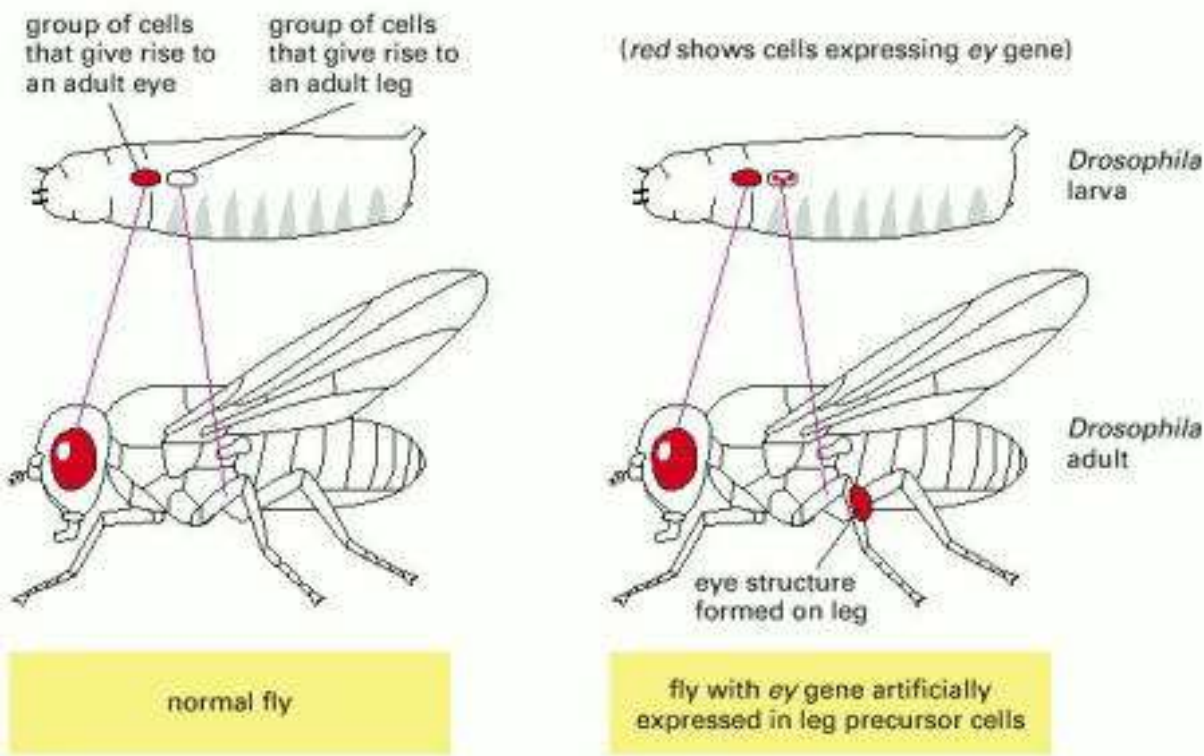
Lens

Cornea

# Lens induction



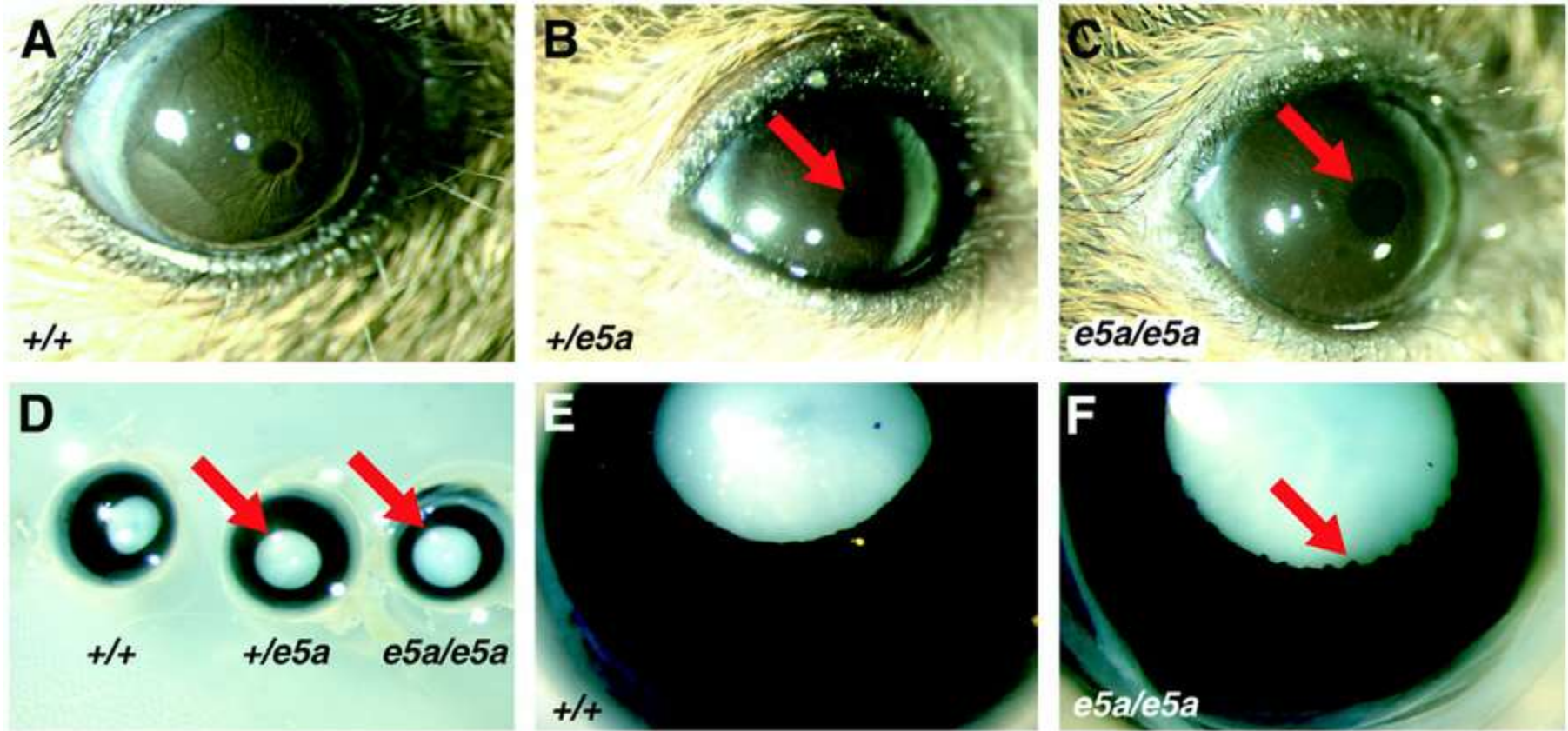
# ey/pax6 can ectopically induce eye formation



(B)



# Pax6 is also important for eye development in mammals



A-C: Eyes of adult wild type (left), Pax6<sup>tm1Gfs</sup>/Pax6<sup>+</sup> (center), and Pax6<sup>tm1Gfs</sup>/Pax6<sup>tm1Gfs</sup> (right) mice. Arrow indicates hypoplasia of the iris with a larger pupil. D: eyes of adult mice after fixation. Black: iris ; white: lens. Arrow: iris hypoplasia. E & F: a homozygous mouse eye (F) showing an irregular iris (arrow) in the pupil region.



# Summary (III)

- Key word:  
eye field, shh, nodal, lens
- Event and mechanism  
eye field separation, lens induction