

*Scientific Literature Analysis In Neuroscience*

EPFL

# **Neurodevelopment – an overview**

**BIOENG-451**

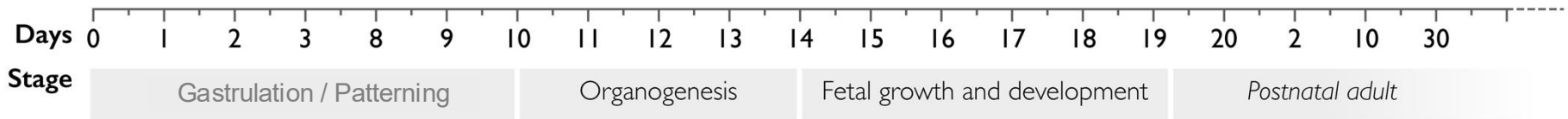
Academic year: 2025-2026

Teacher: Prof. Gioele La Manno

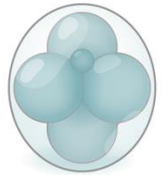
TA: Alessandro Valente

- Brain developmental timeline
- Neurulation and patterning
- Gene networks regulating neurogenesis
- Temporal and spatial interplay of gene expression and morphogens secretion

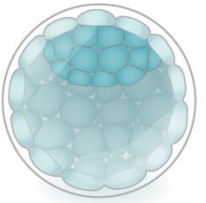
# Development Timeline



50  
ts1



50  
ts3



100  
ts6



150  
ts9



150  
ts11



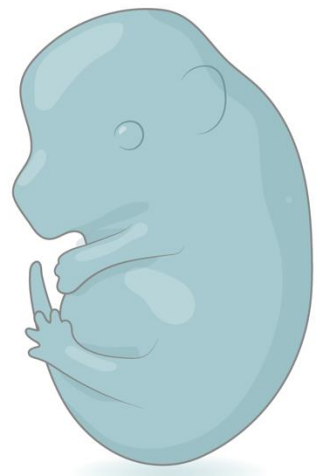
200  
ts14



1000  
ts18

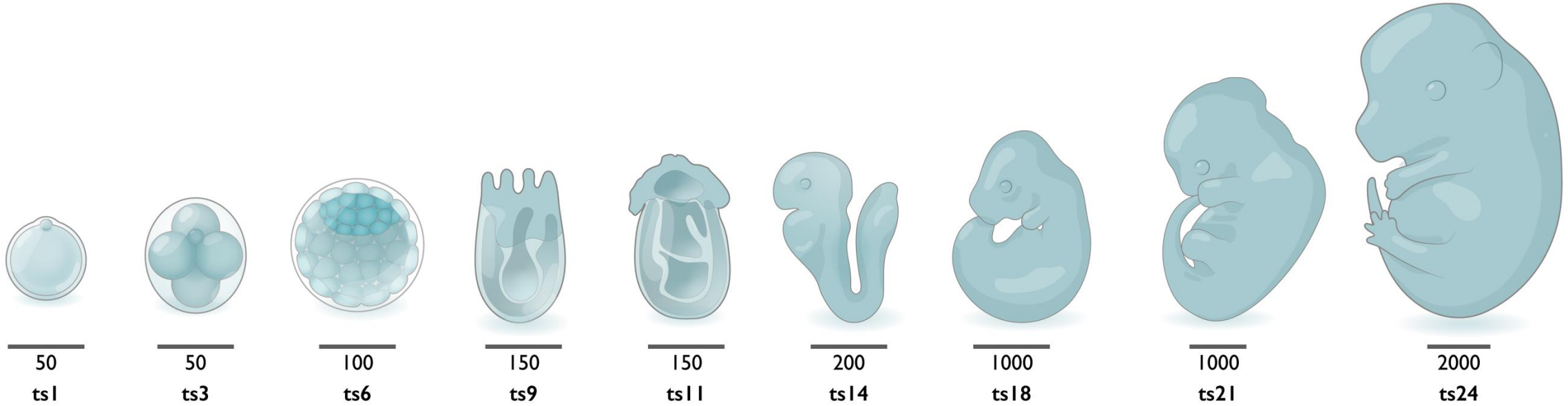
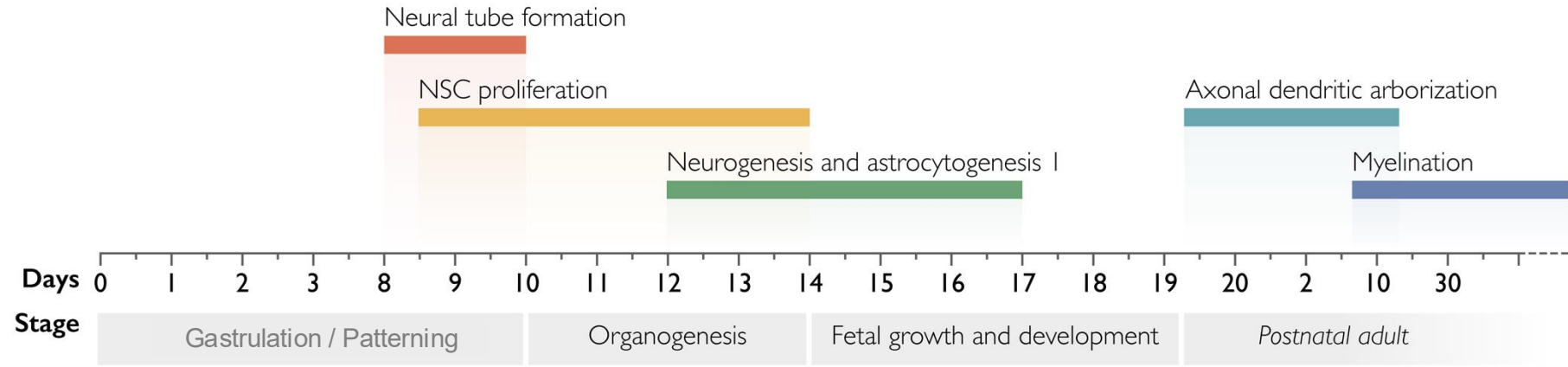


1000  
ts21



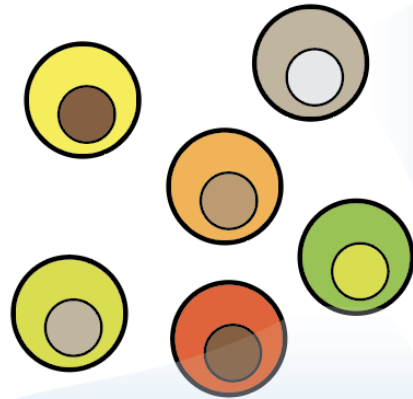
2000  
ts24

# Development Timeline

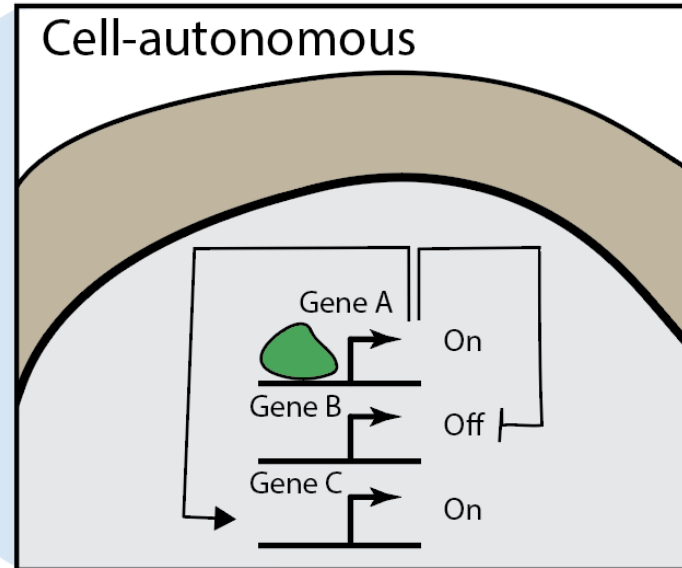


# Rules and Processes

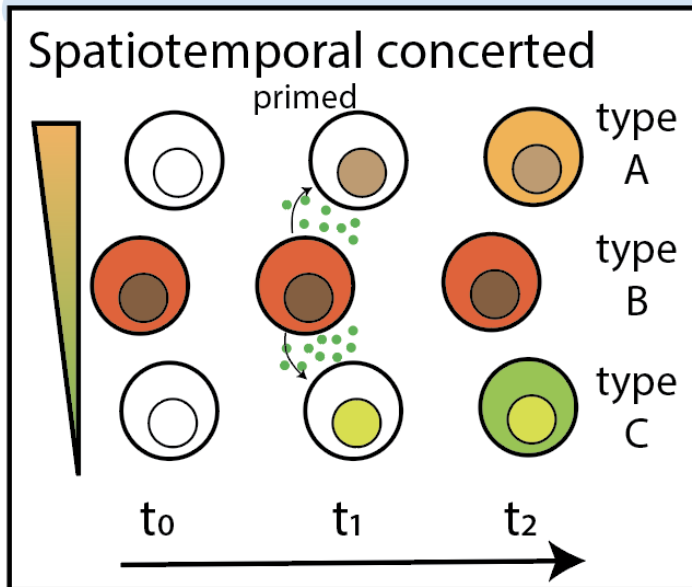
Cell population



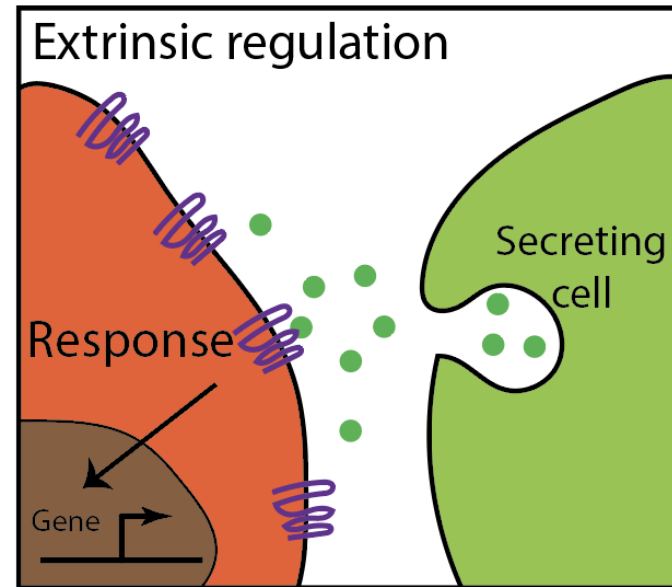
Cell-autonomous



Spatiotemporal concerted



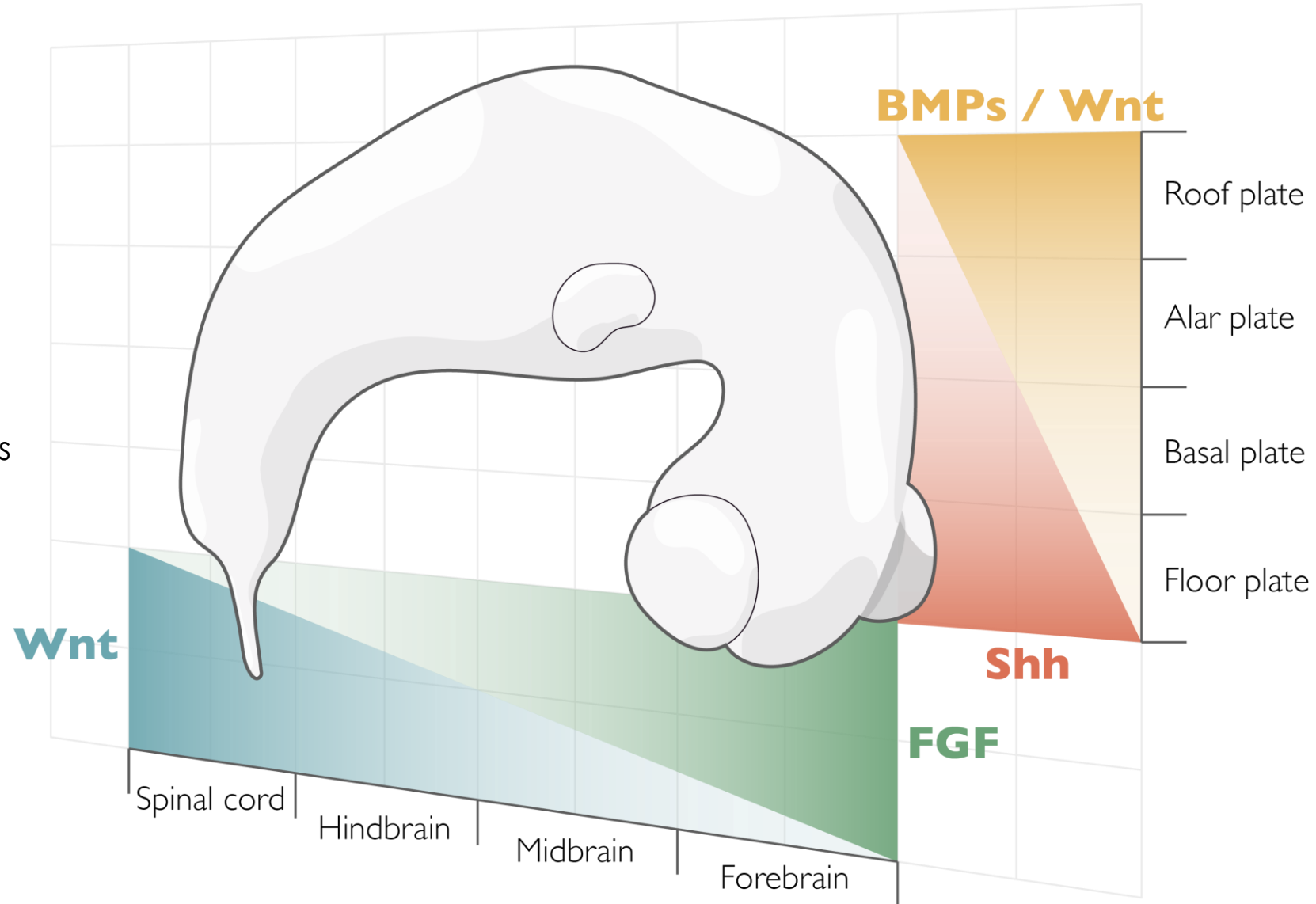
Extrinsic regulation



# Developmental cues

## Signaling molecules:

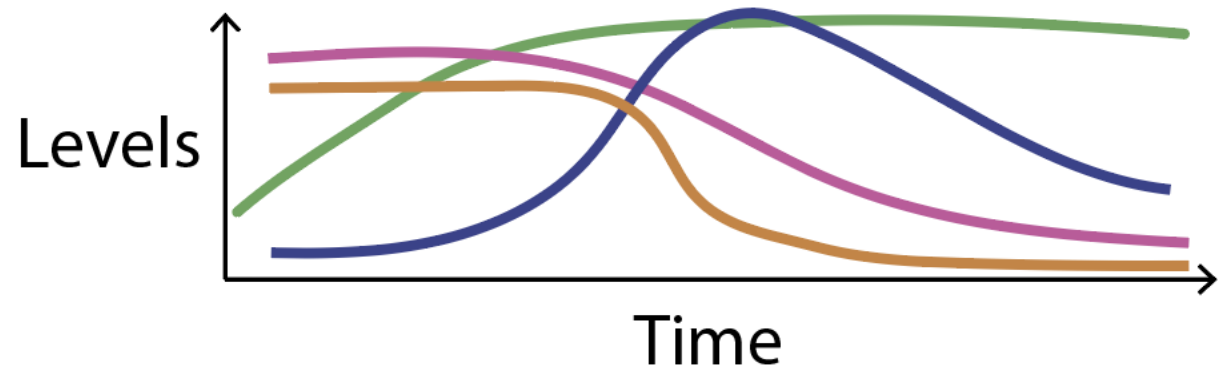
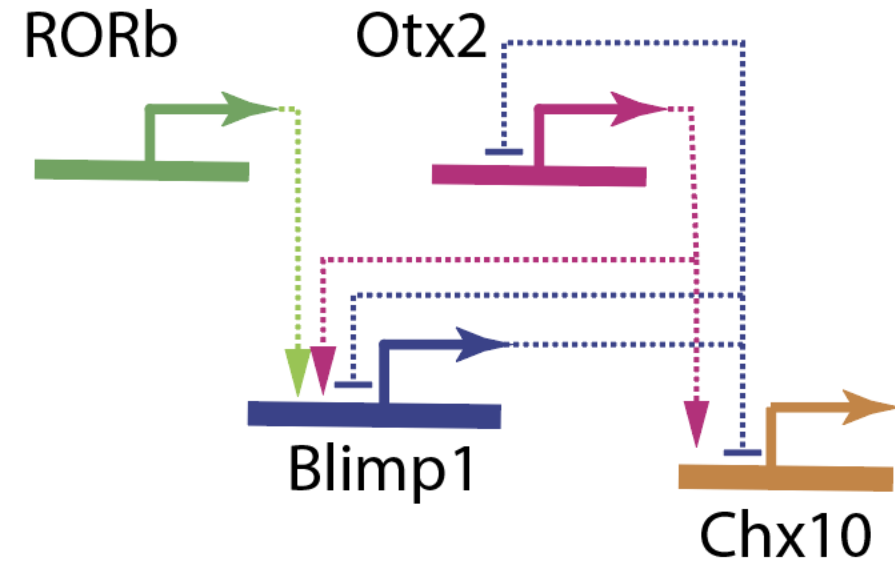
- Restrict the fate of progenitors cells
- Define axes and anatomical regions
- Different roles at different times



# Regulatory networks

## Gene regulatory networks

- Determine a temporal unfolding of events
- Establish lock-in steady states corresponding to endpoints of developments
- Can be simulated using differential equations



# Regulatory networks

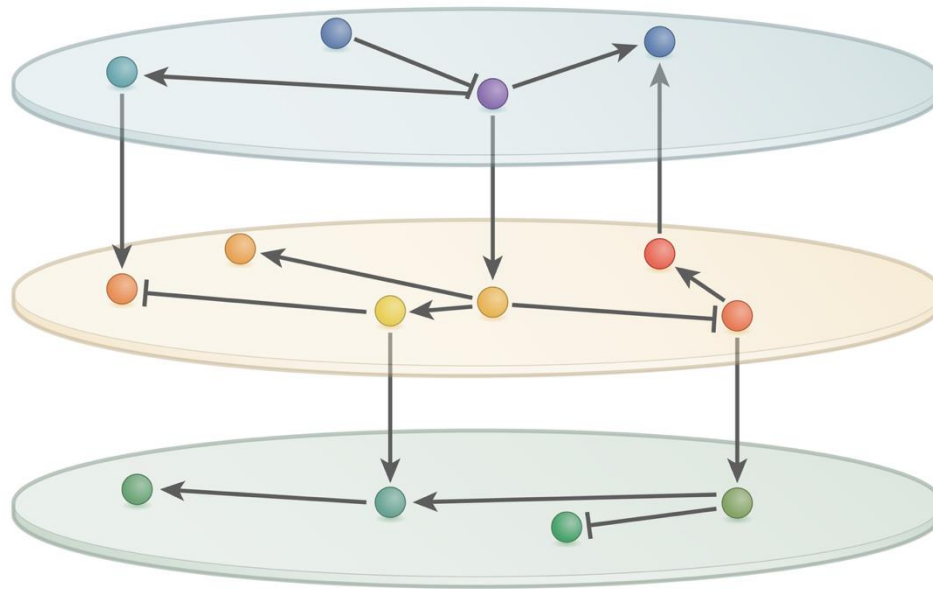
**Complex morphogenetic processes** arise from the combination of regulation of:

- different biological processes within a cell
- different cells/lineages/tissues

Neural progenitor proliferation vs differentiation

Forebrain territory specific program

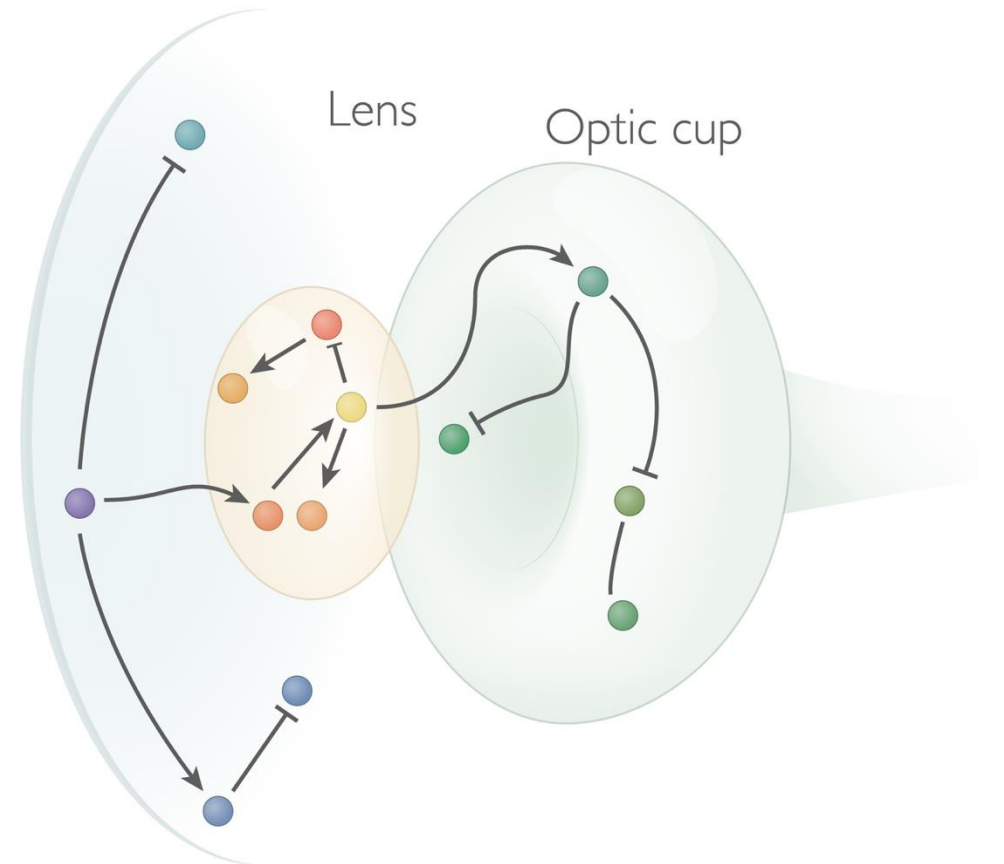
Cell polarity and conversion-extension movements



Periocular mesenchyme

Lens

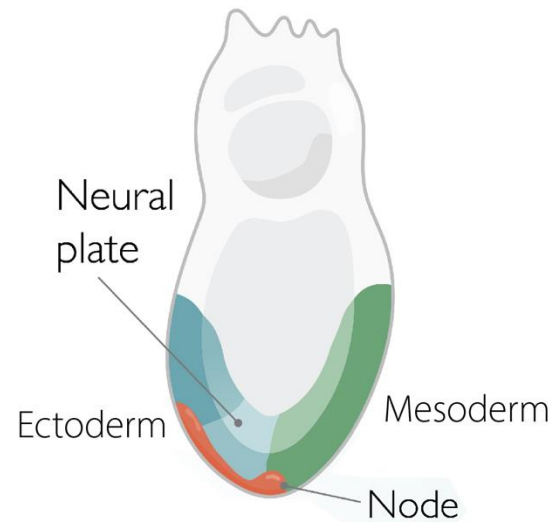
Optic cup



# Stages of neurodevelopment

## Early induction and Neurulation

At the end of gastrulation  
Mouse E7.5 – E10.00



# Stages of neurodevelopment

## **Early induction and Neurulation**

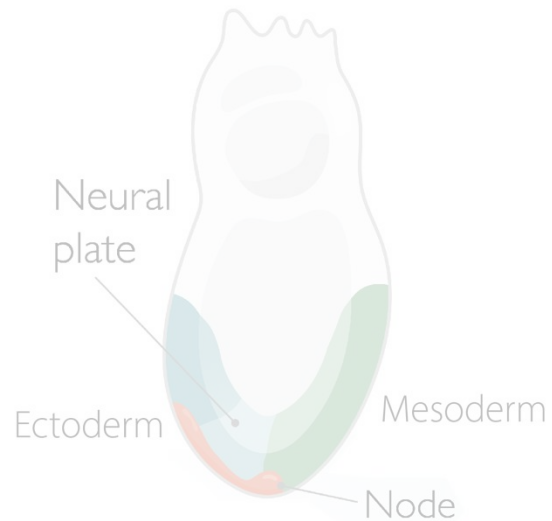
At the end of gastrulation  
Mouse E7.5 – E10.00

- Induction of the neuroectoderm
- Neural plate regionalization
- Neural tube closure
- Definition of the 3 vesicles
- Definition of secondary organizers

# Stages of neurodevelopment

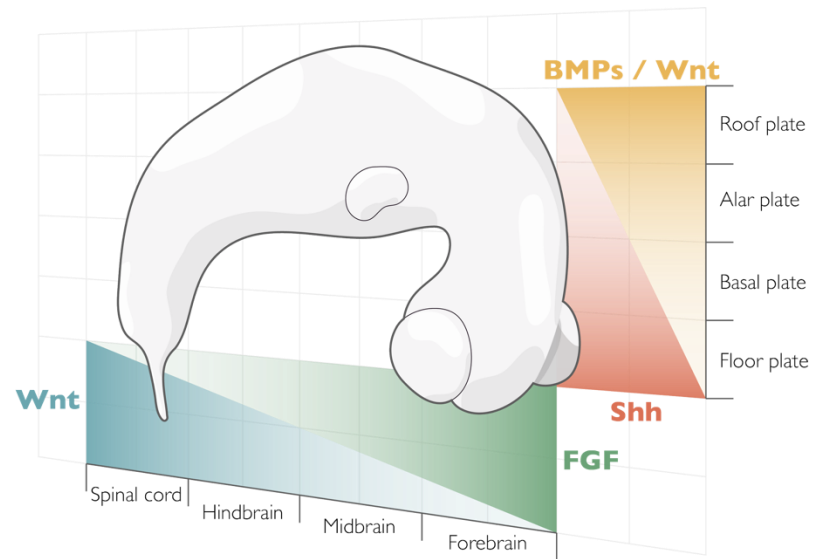
## Early induction and Neurulation

At the end of gastrulation  
Mouse E7.5 – E10.00



## Embryonic development

After neural tube closure  
Mouse E10 – E18



# Stages of neurodevelopment

## Early induction and Neurulation

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- Induction of the neuroectoderm
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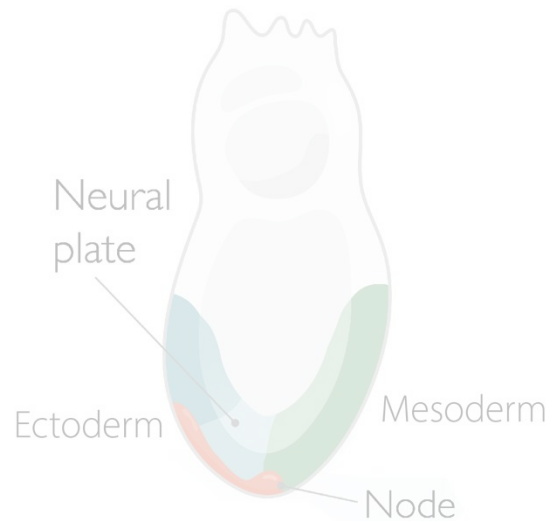
After neural tube closure  
Mouse E10 – E18

- Cell proliferation at the ventricular zone
- Generation of the anatomical complexity
- Fate commitment and differentiation of neurons
- Migration of neuroblasts and glia
- Stratification of the cortex
- Axon growth and segmentation

# Stages of neurodevelopment

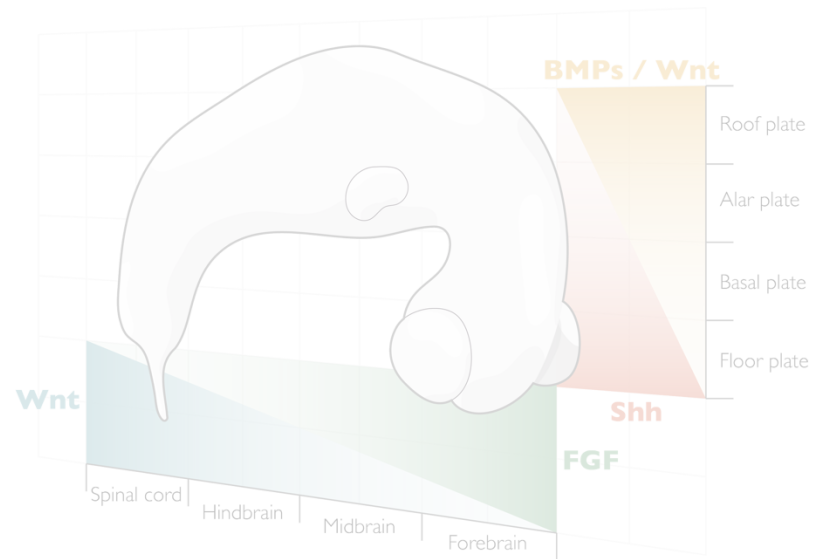
## Early induction and Neurulation

At the end of gastrulation  
Mouse E7.5 – E10.00



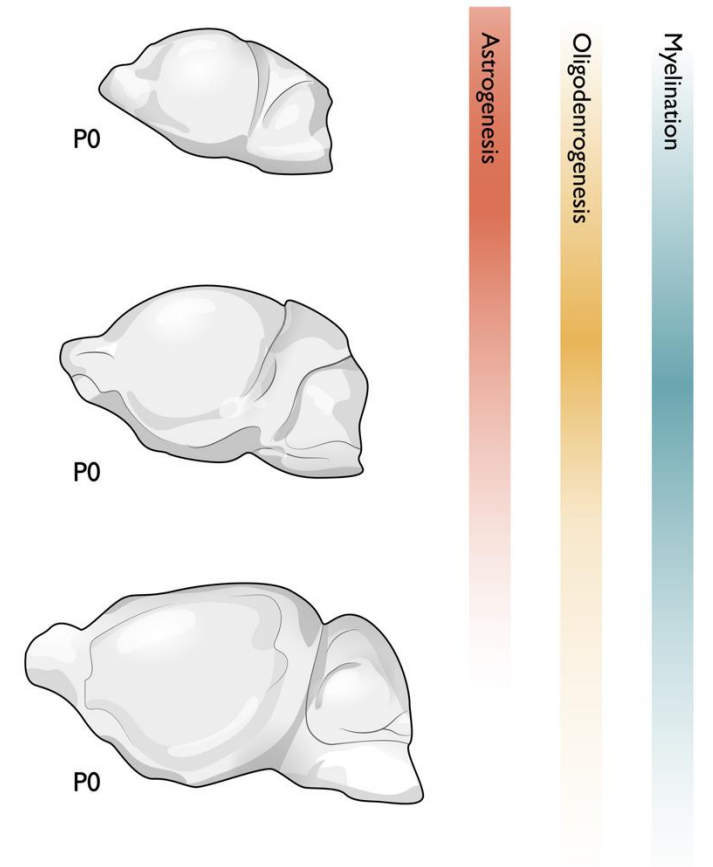
## Embryonic development

After neural tube closure  
Mouse E10 – E18



## Postnatal brain development

From birth to adulthood



# Stages of neurodevelopment

## Early induction and Neurulation

At the end of gastrulation  
Mouse E7.5 – E10.00

- Induction of the neuroectoderm
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After neural tube closure  
Mouse E10 – E18

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## Postnatal brain development

From birth to adulthood

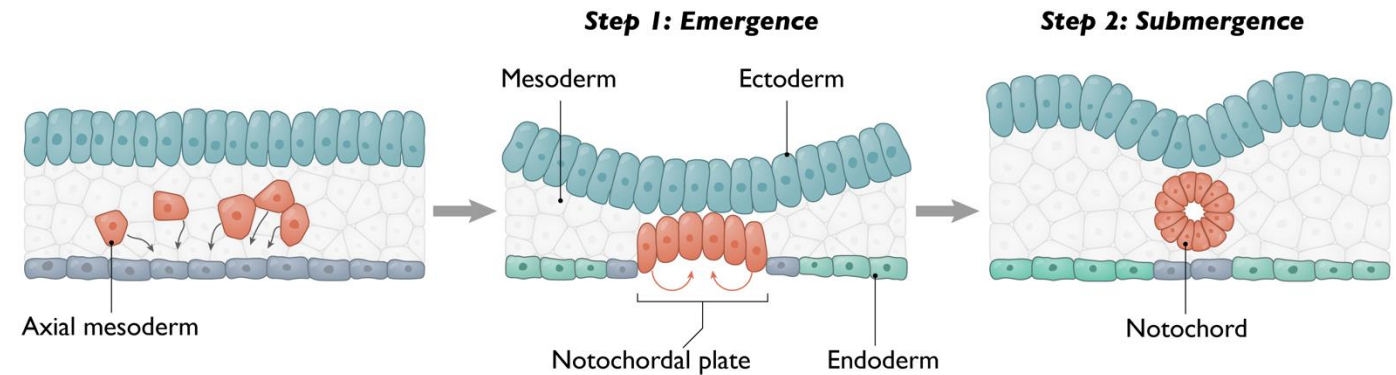
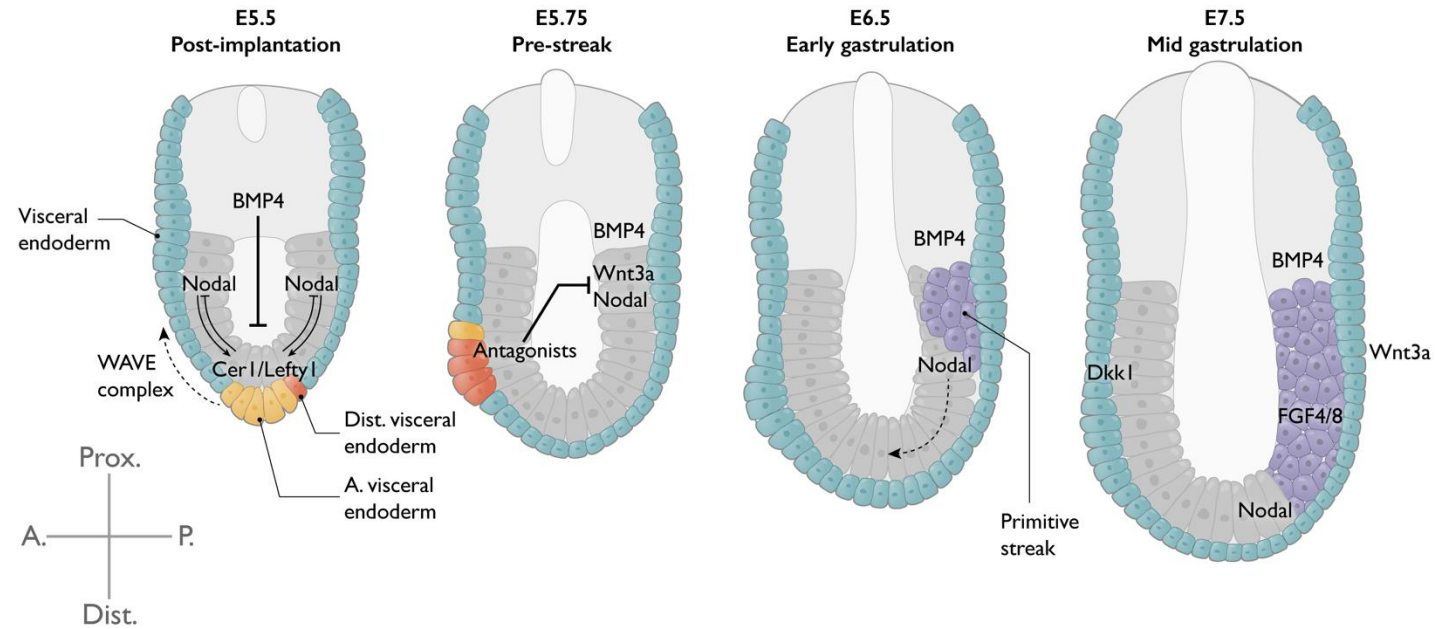
- Completion of gliogenesis
- Fine tuning of neuronal subtypes
- Definition of synaptic contacts
- Neurogenesis in particular areas

# Gastrulation

Gastrulation is the starting point for nervous system development.

The gastrulation process has already:

- Broken symmetry defining AP and DV axes
- Defined the three embryonic germ layers
- Produced the notocord



# Gastrulation

## Gastrulation

### Mouse embryo

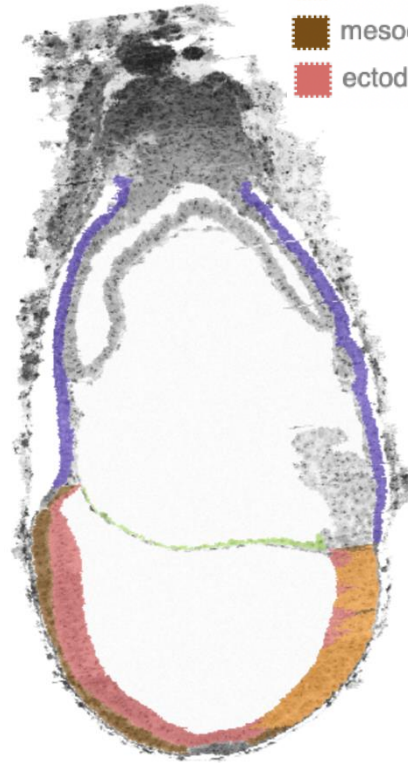
3d View

- primitive streak
- mesoderm
- ectoderm



Sagittal Plane

- visceral endoderm
- amnion mesoderm
- primitive streak
- mesoderm
- ectoderm



Anterior - Posterior

# Early induction

## Gastrulation

### Mouse embryo

3d View

Sagittal Plane

- primitive streak
- mesoderm
- ectoderm

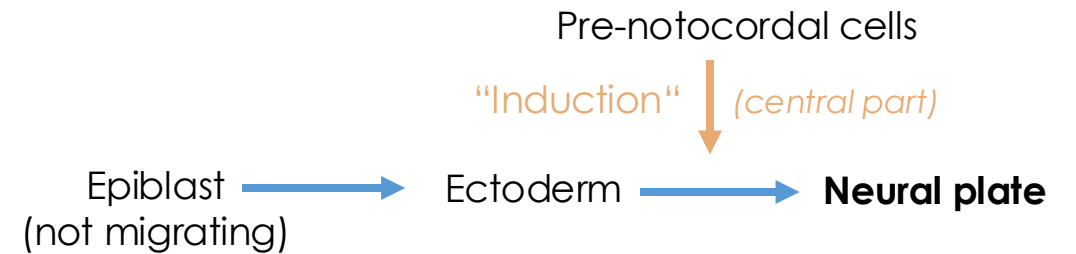


- visceral endoderm
- amnion mesoderm
- primitive streak
- mesoderm
- ectoderm

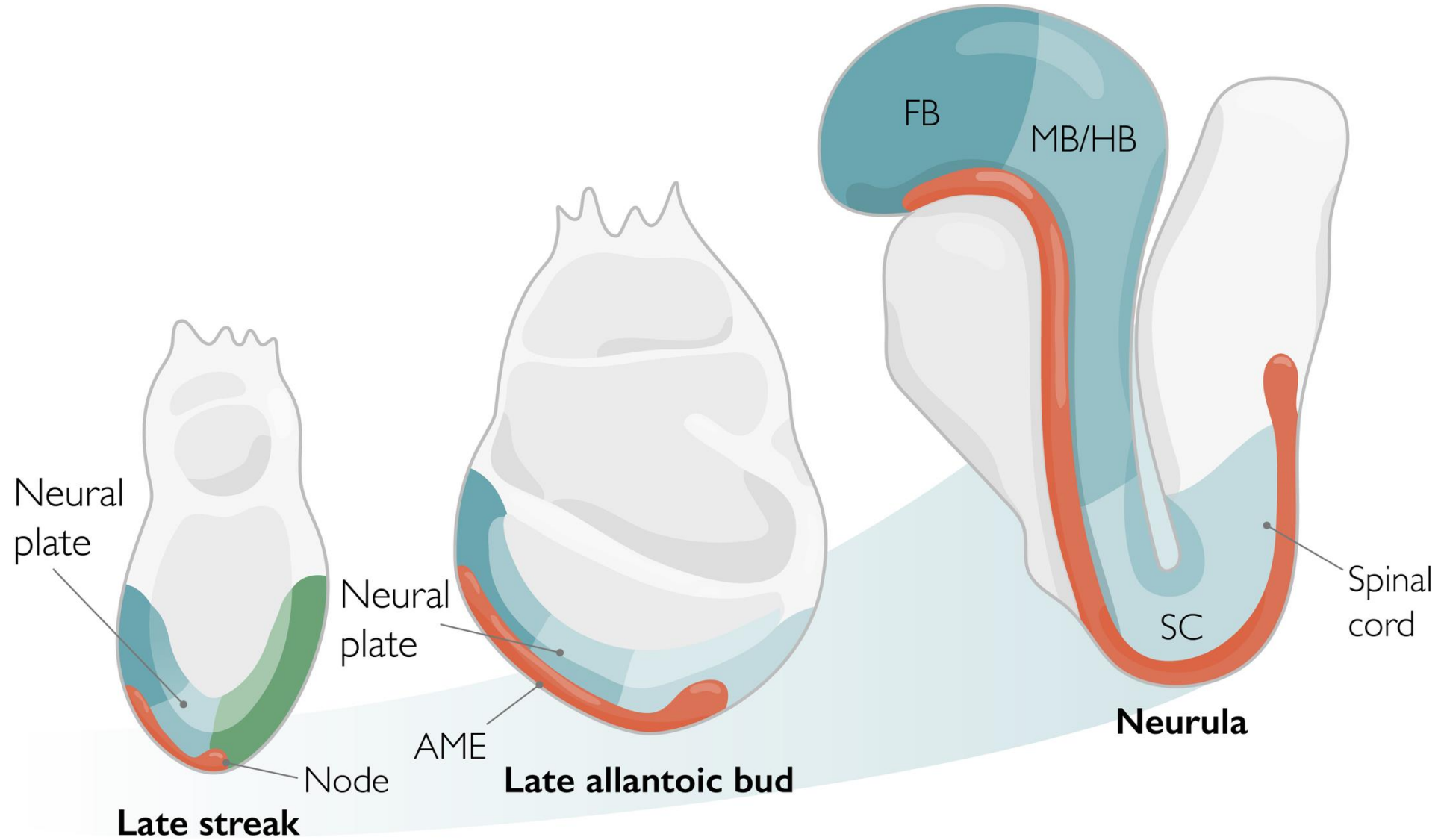


Anterior - Posterior

## Neuroectoderm "induction"



# Brain vesicles formation

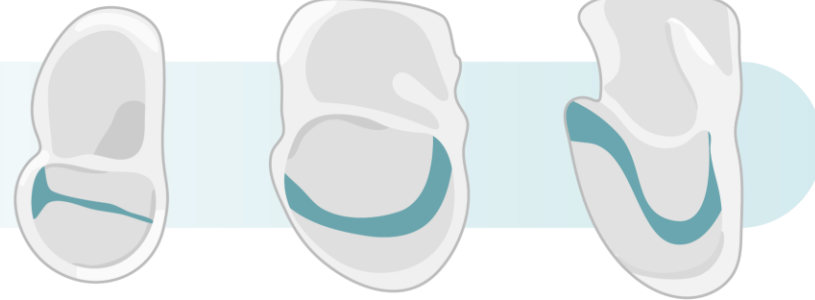


# Patterning signals

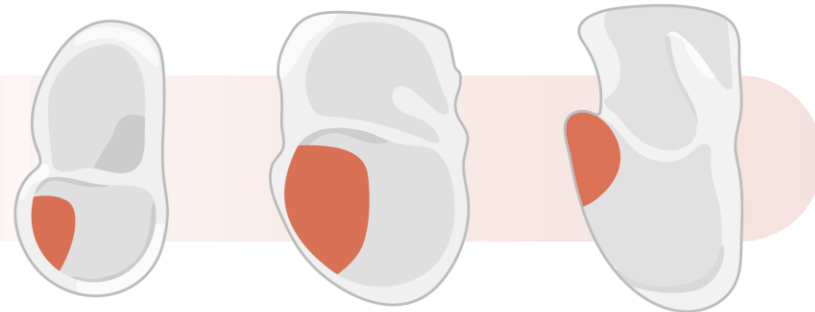
Patterning signals

Neural plate    Headfold    Late headfold

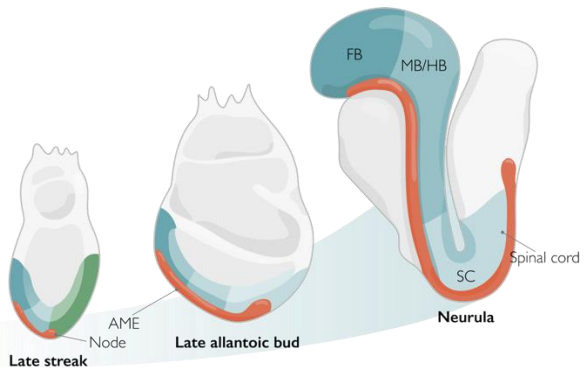
Dlx5



Hesx1

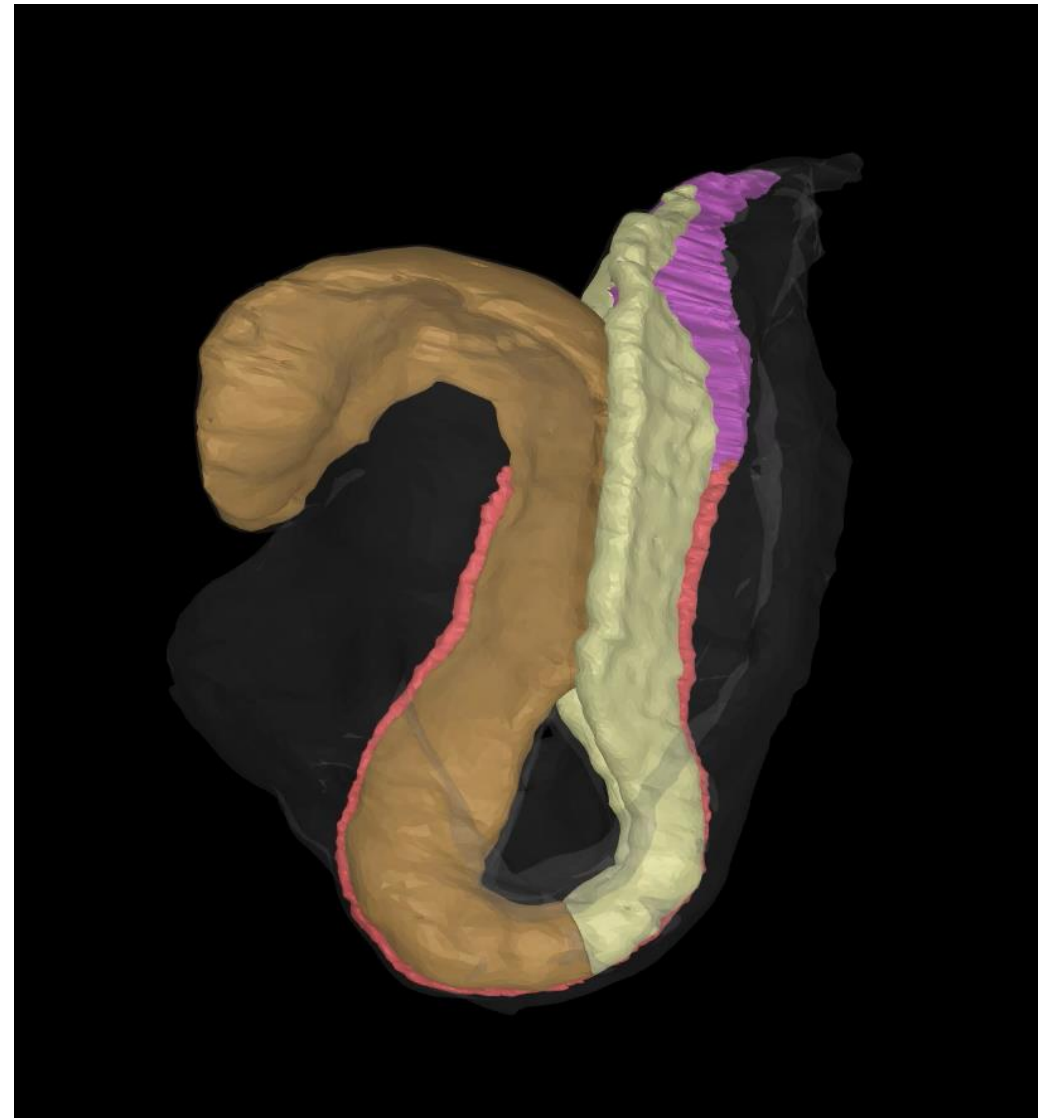


Sox1



# Patterning signals

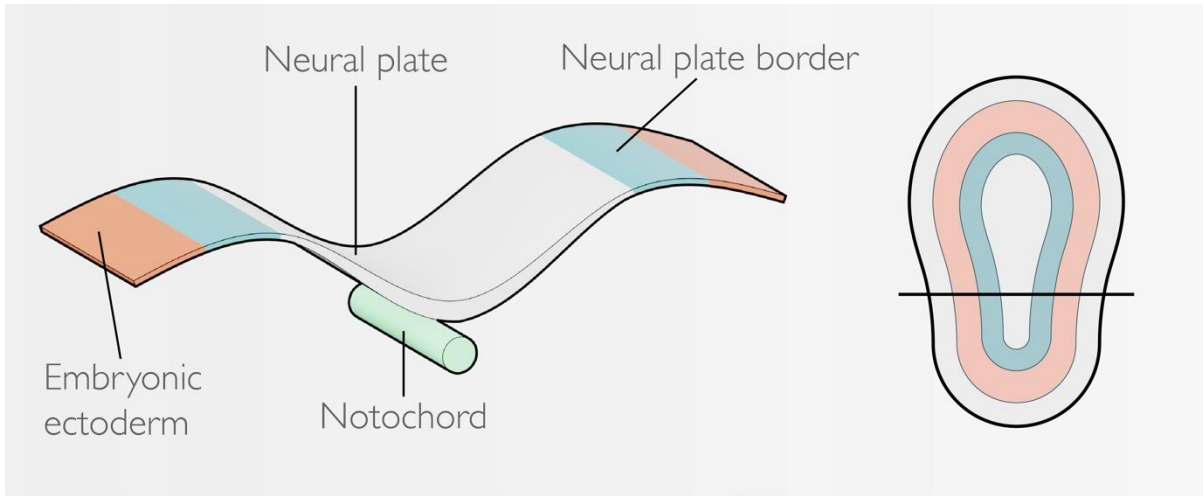
The neural plate at E8.25:



primitive streak    neural tube  
notochord    future brain

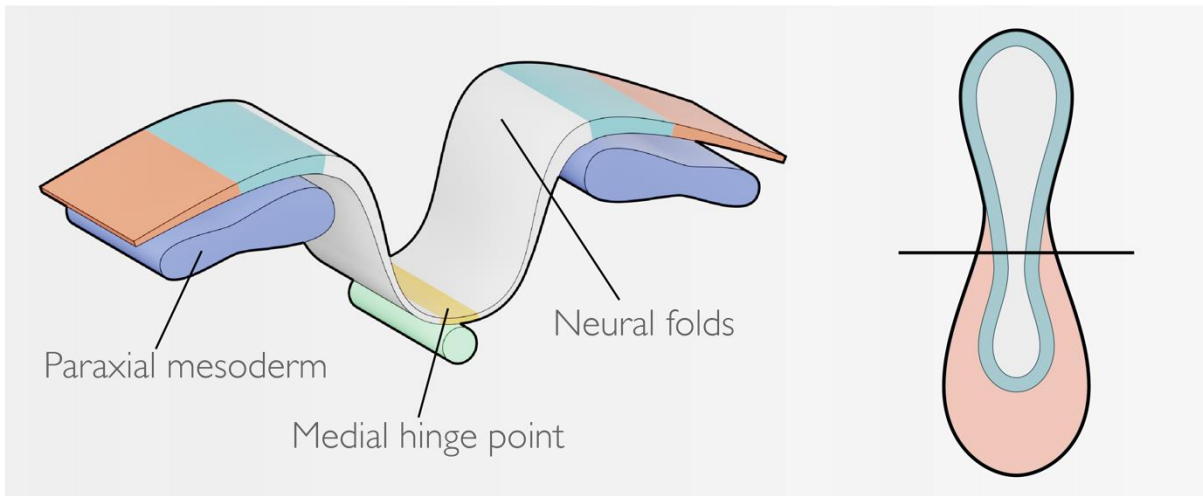
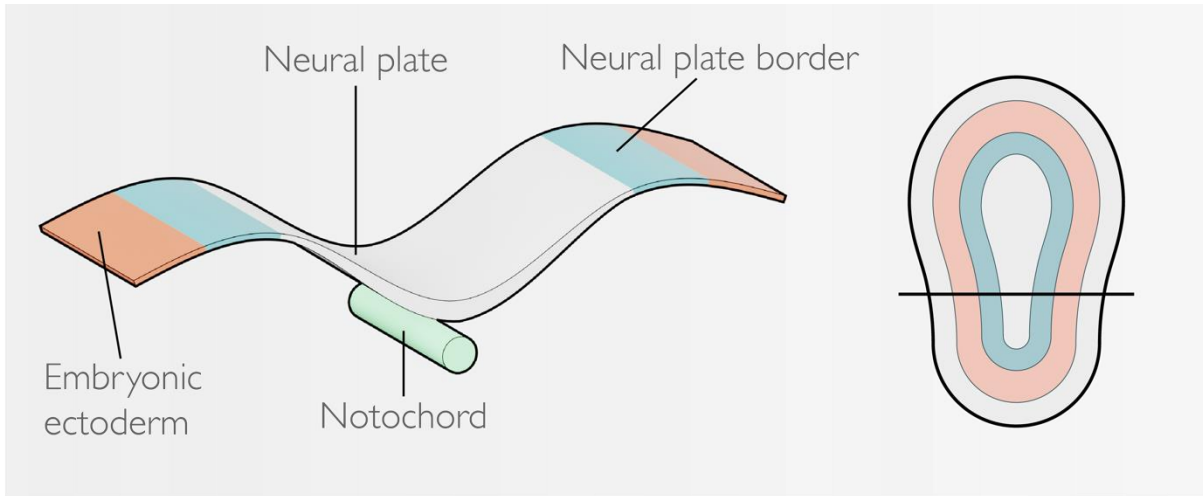
# Neurulation

**Neurulation:** process of formation of the folding of the **neural plate** into a **neural tube**.



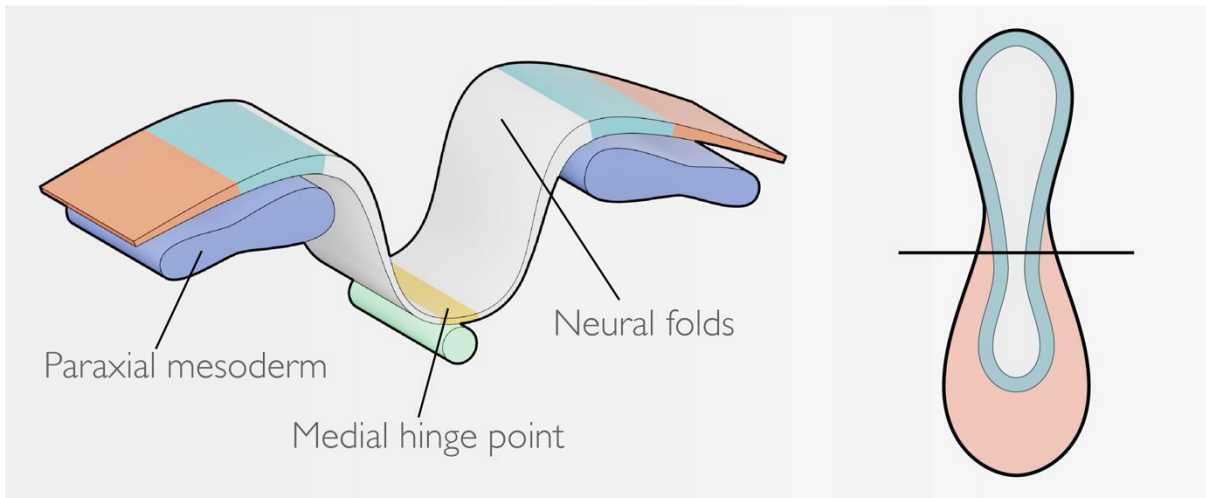
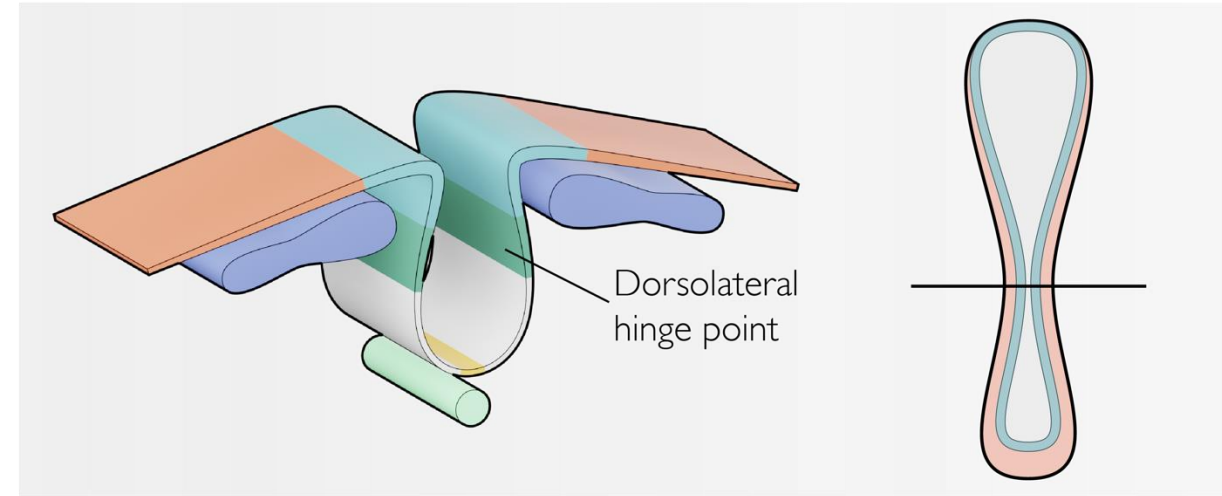
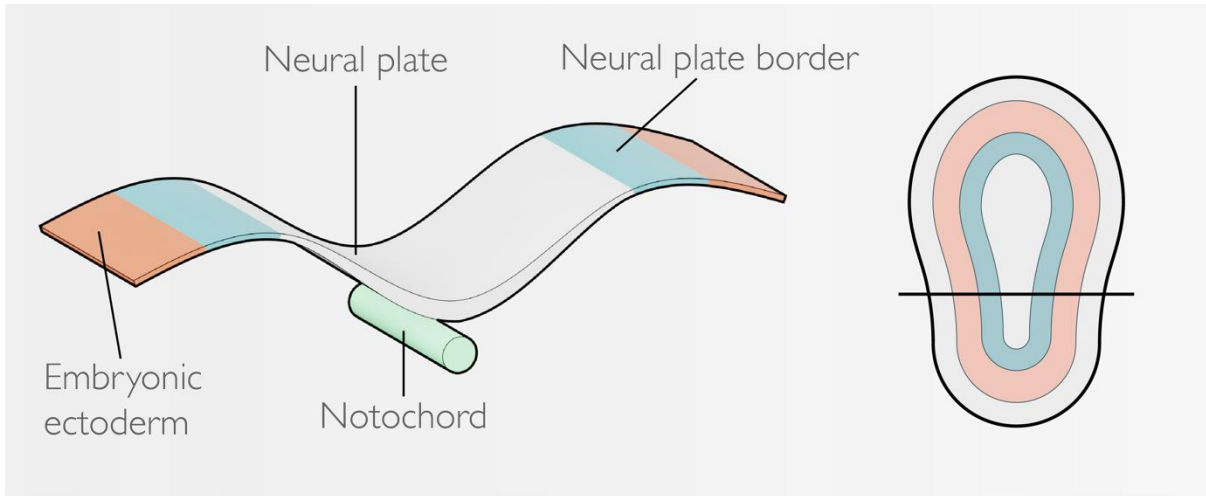
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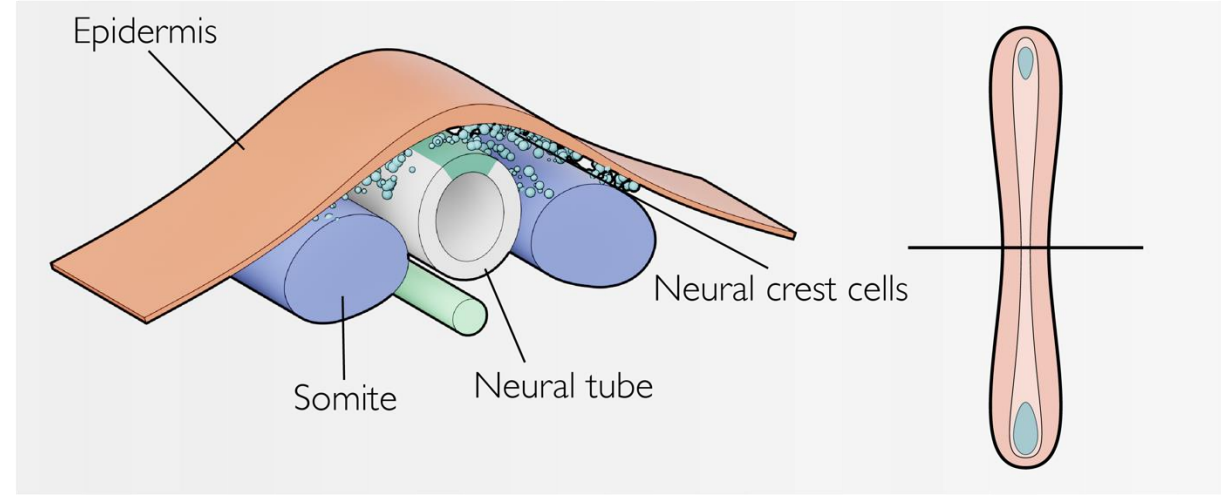
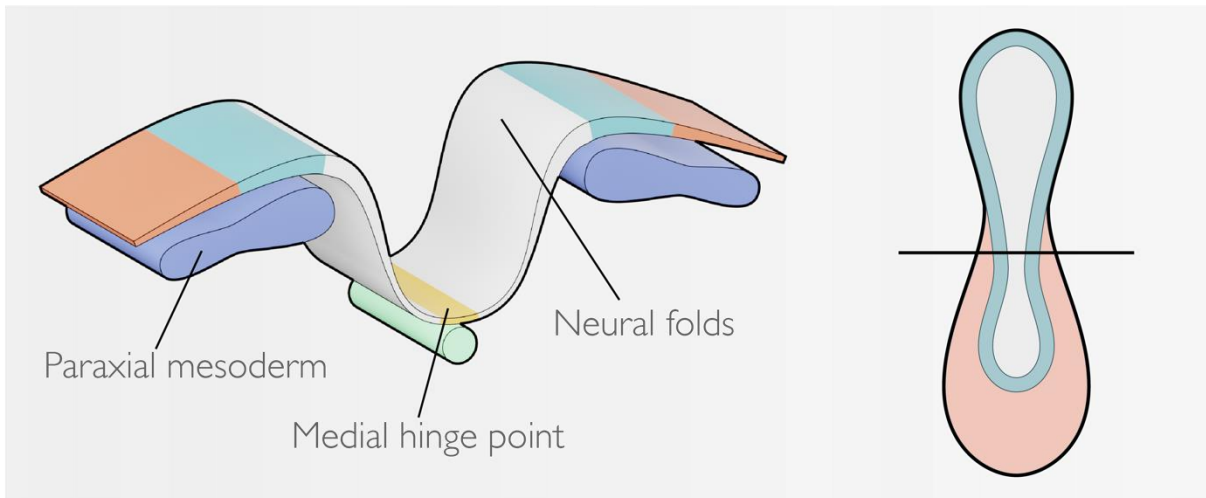
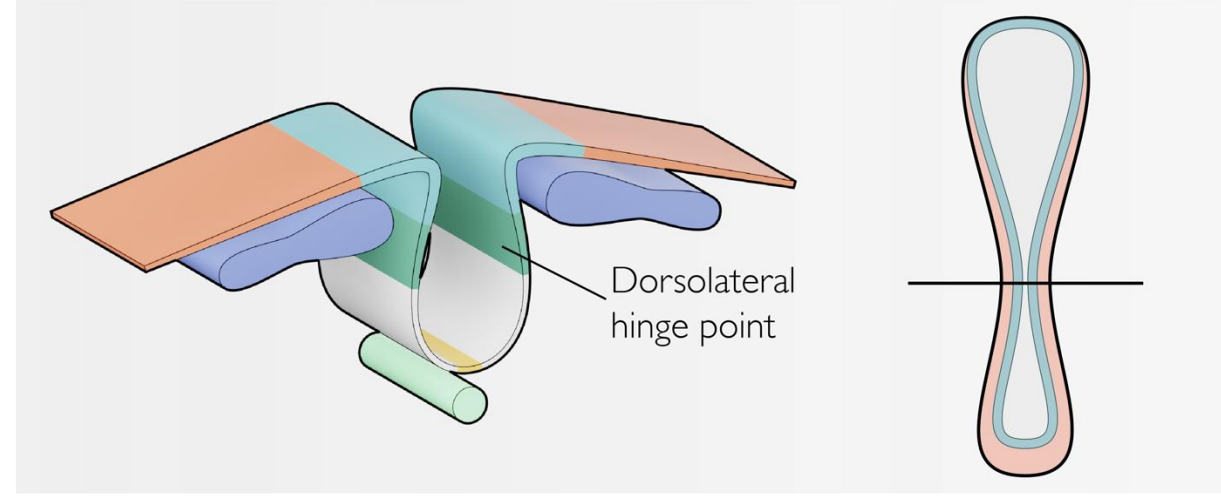
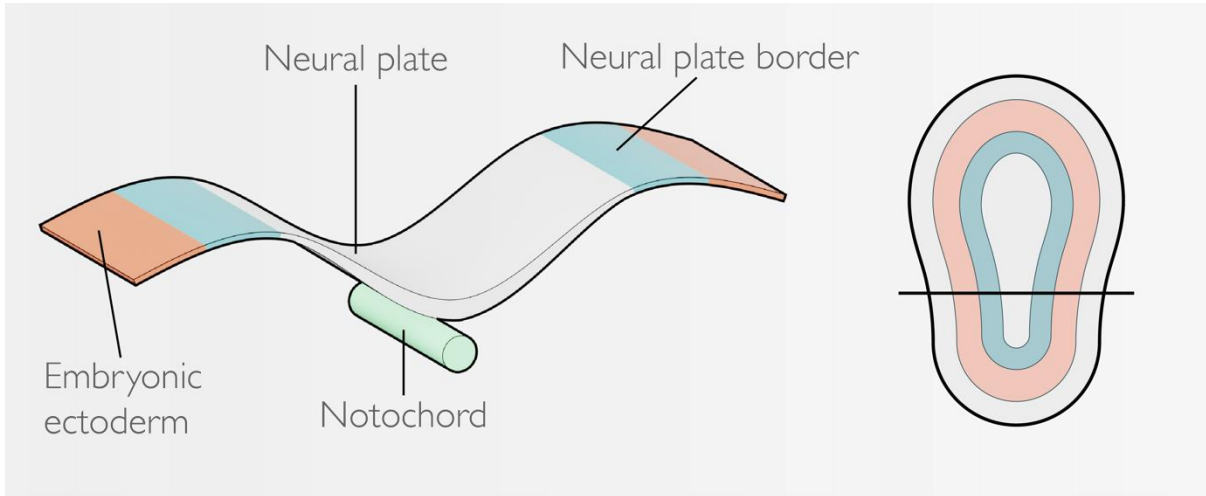
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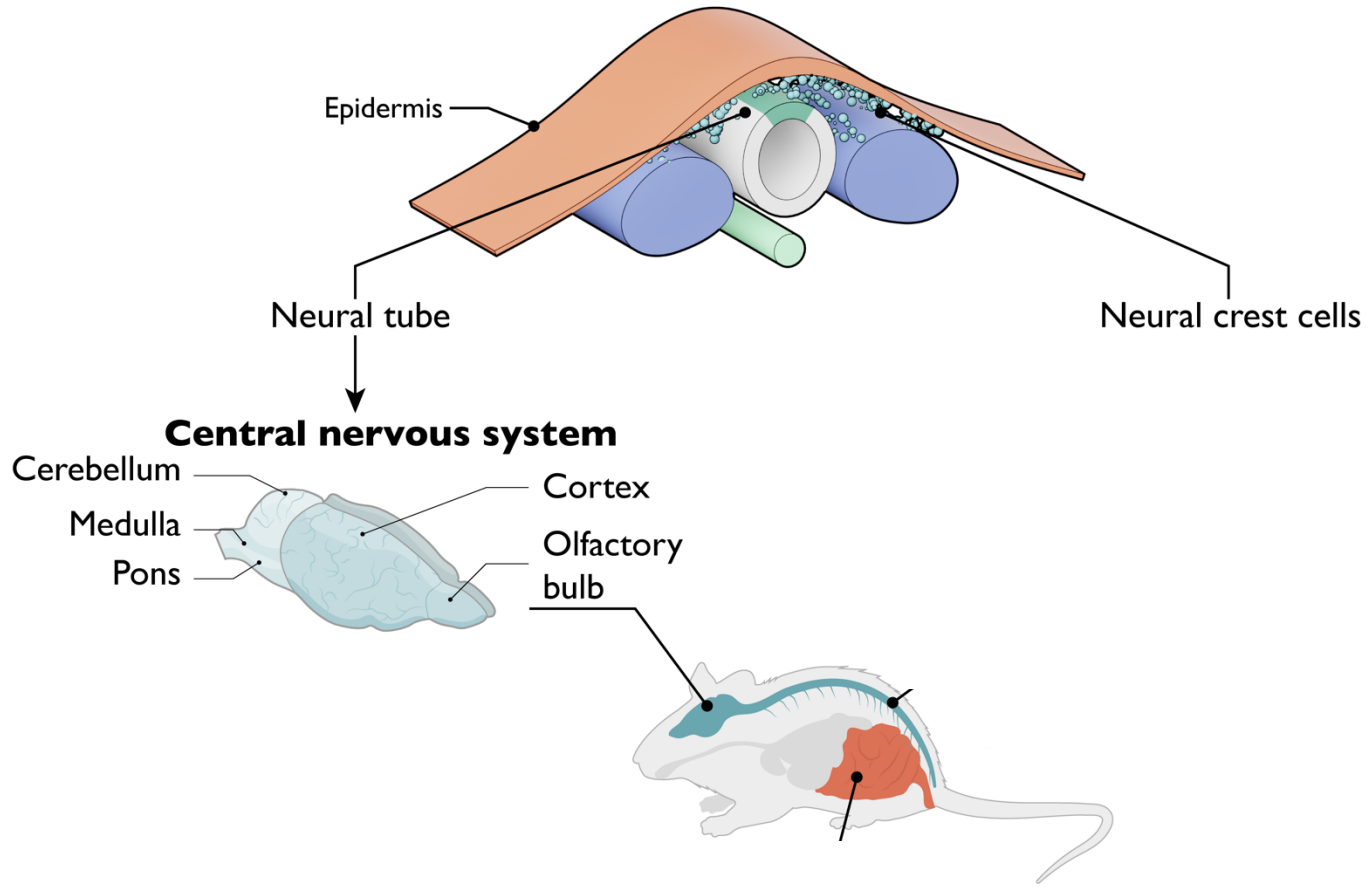


# Neurulation

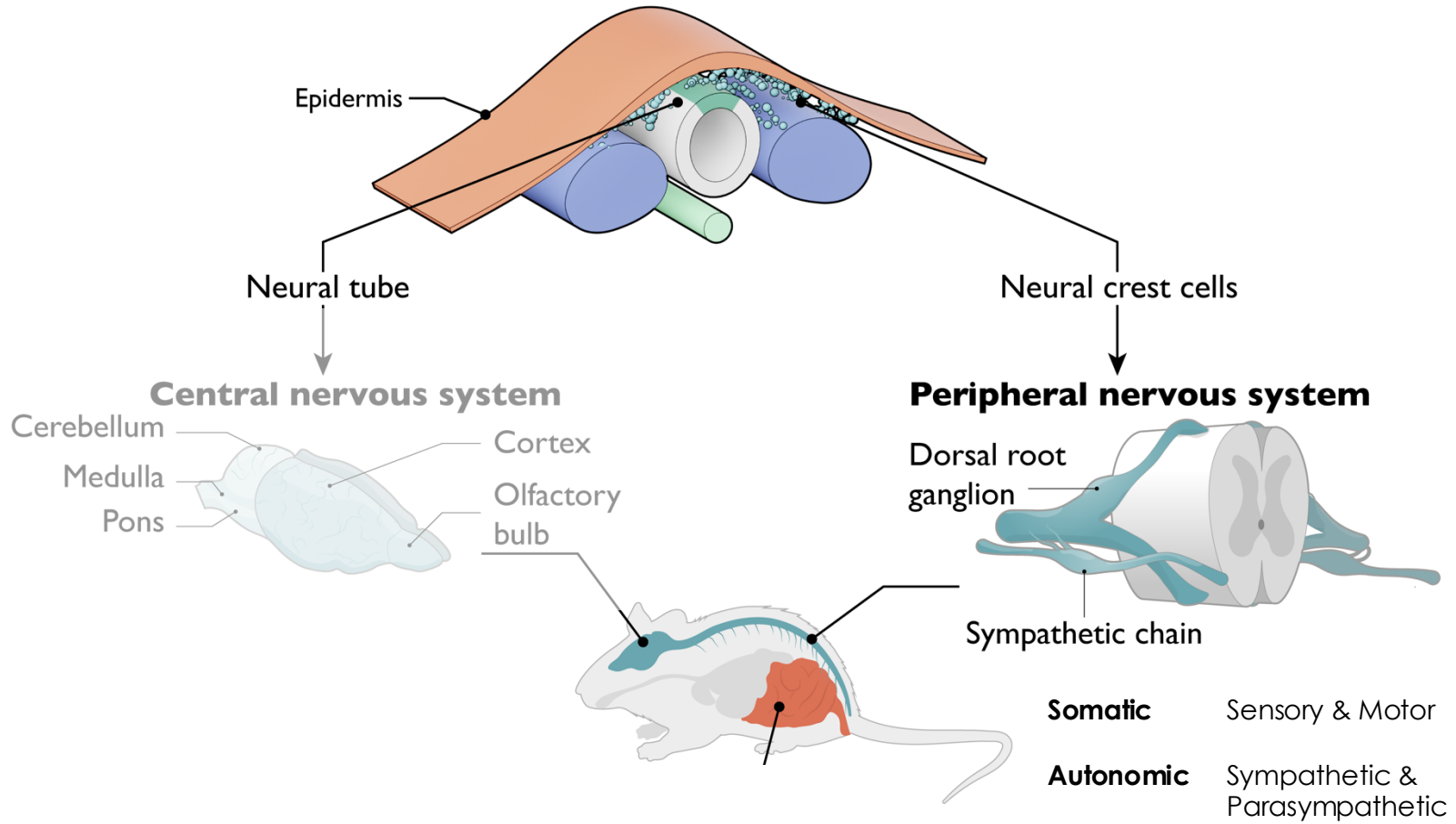
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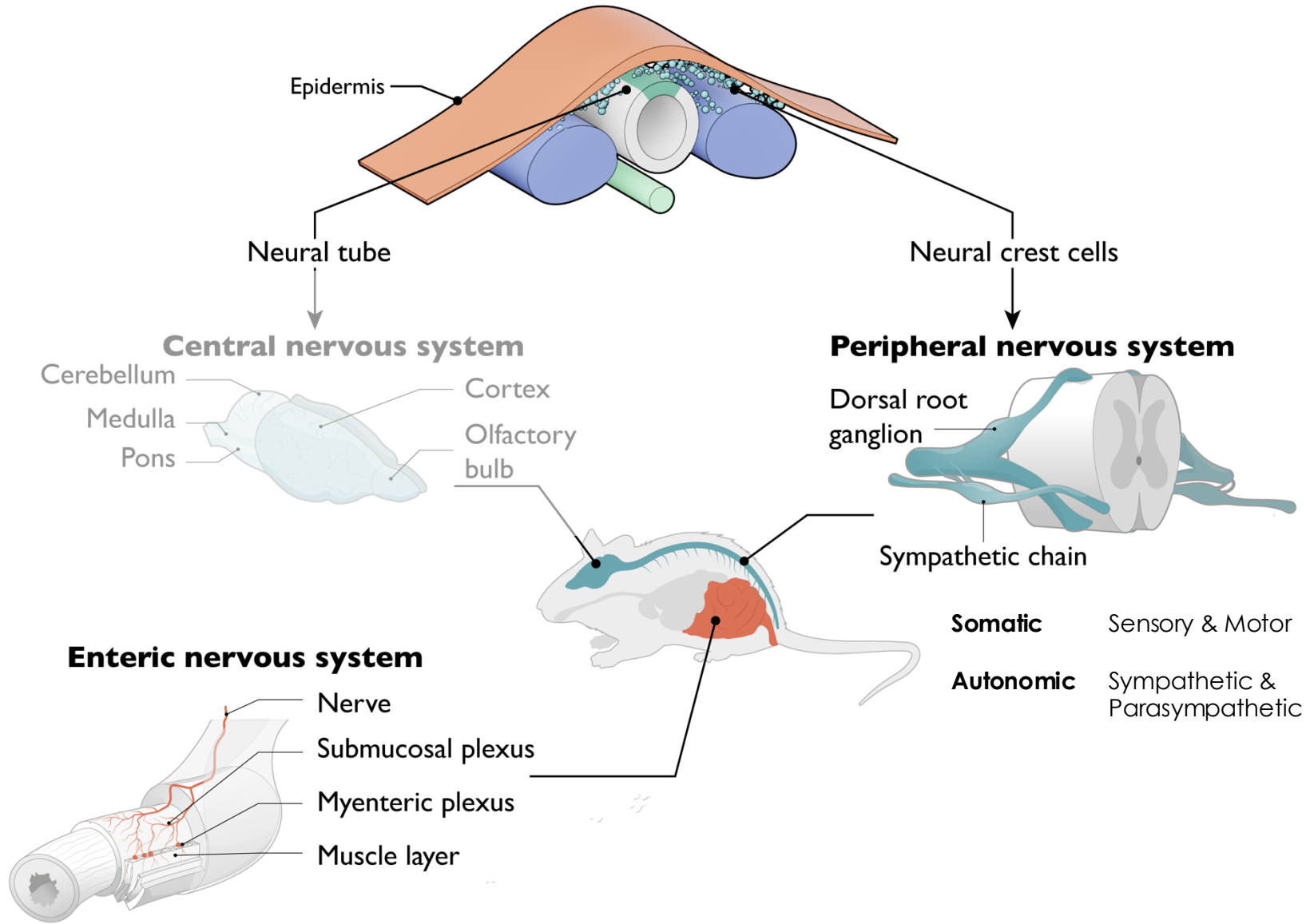
# Neural crest cells



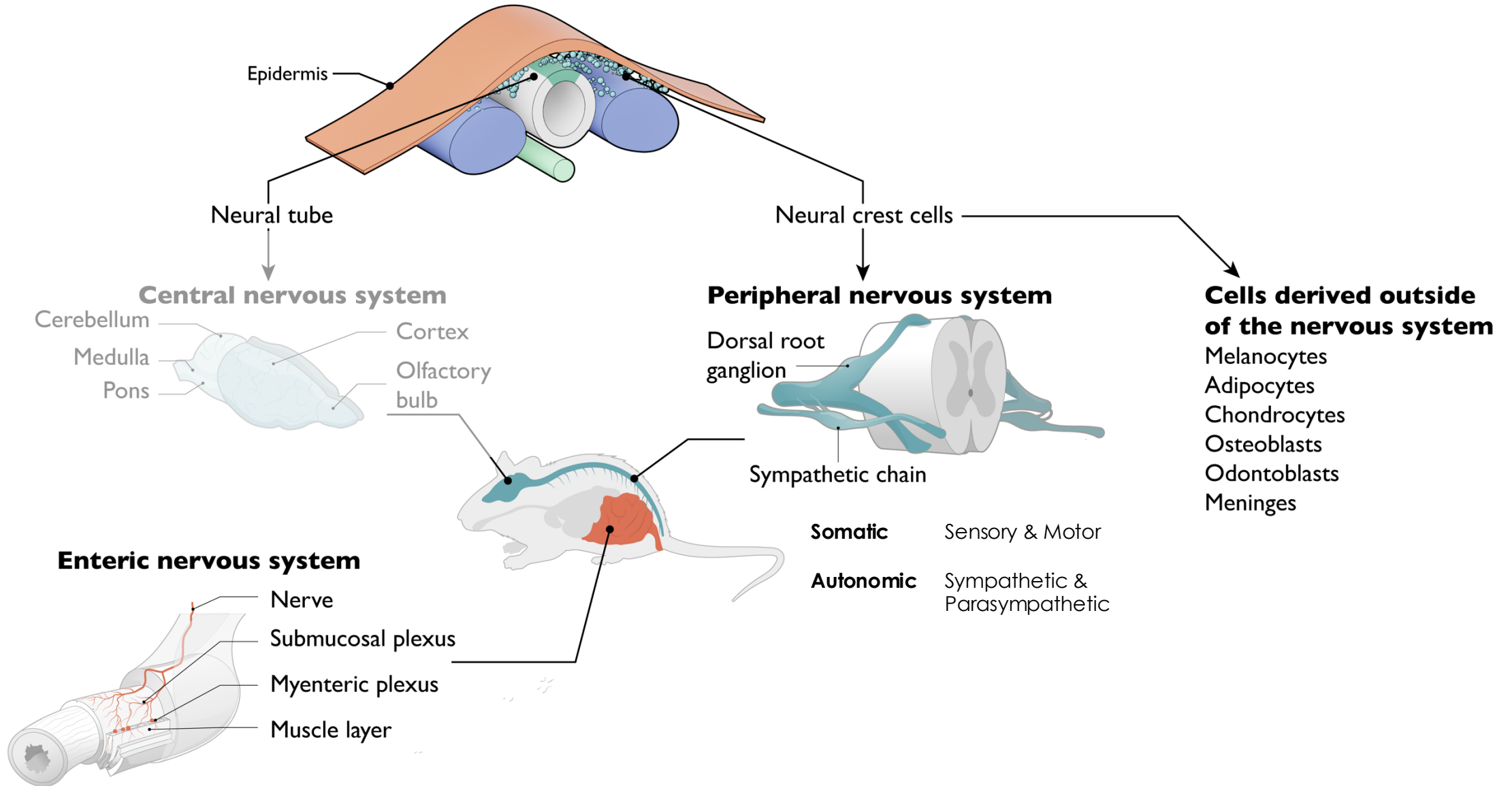
# Neural crest cells



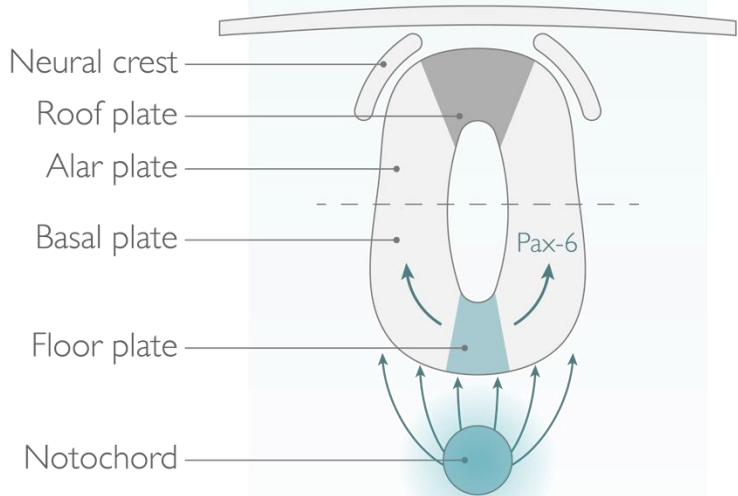
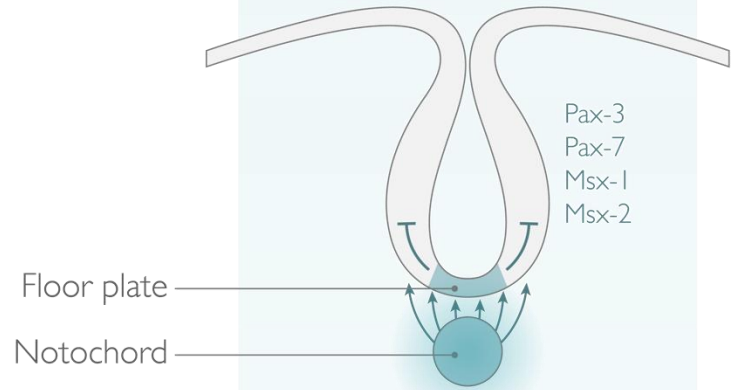
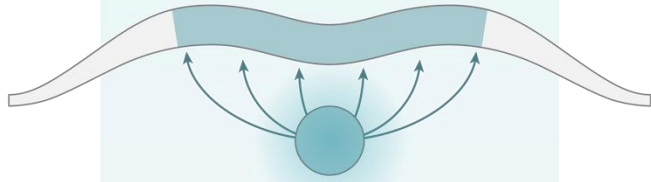
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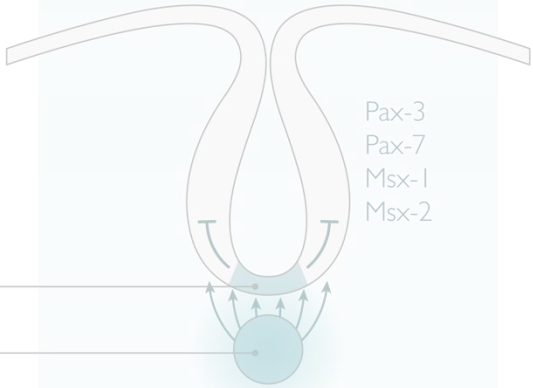
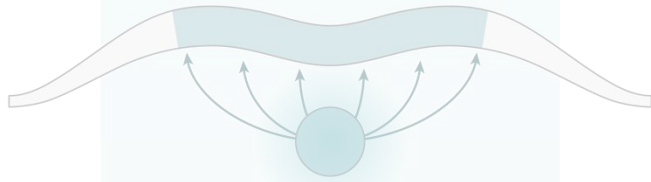
# Neural crest cells



# Shh



# Shh



Pax-3  
Pax-7  
Msx-1  
Msx-2

Floor plate

Notochord

Neural crest

Roof plate

Alar plate

Basal plate

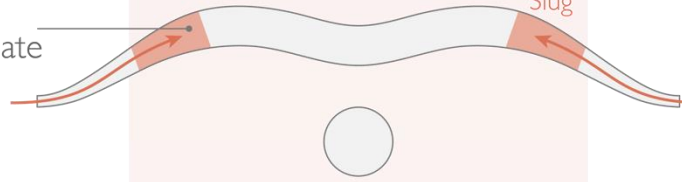
Floor plate

Notochord

Pax-6

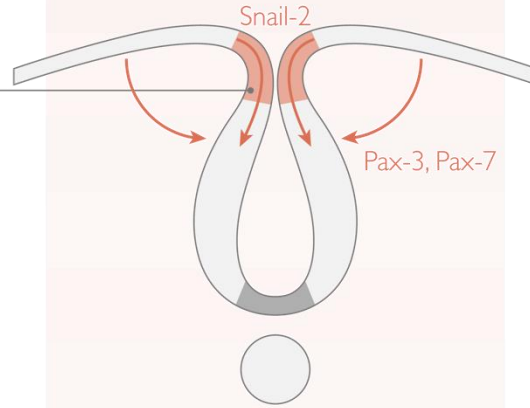
# BMPs

Future  
neural plate



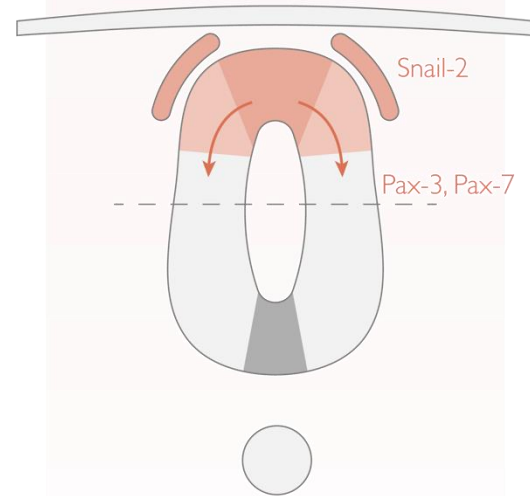
BMP-4  
BMP-7

Neural plate



Snail-2

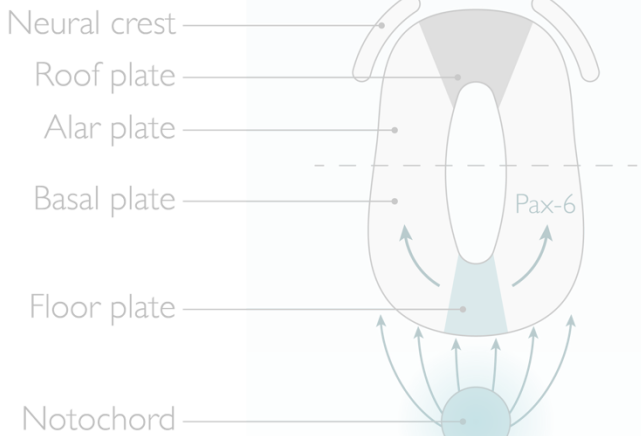
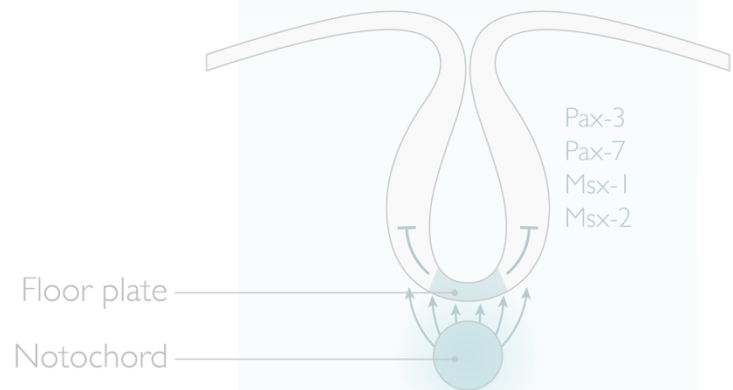
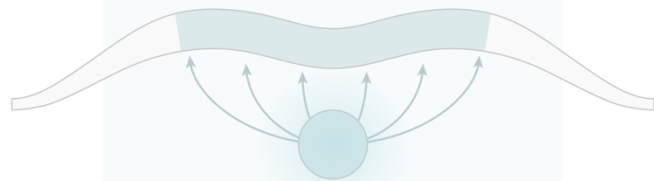
Pax-3, Pax-7



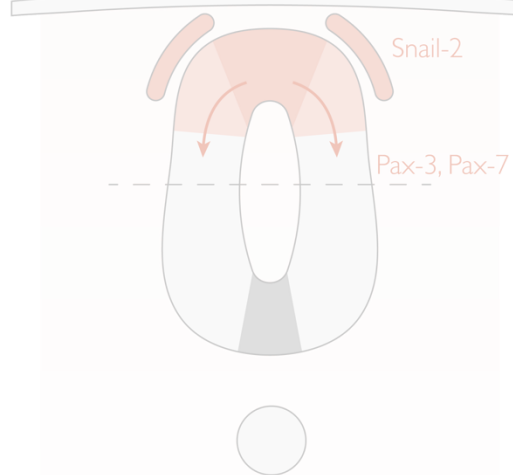
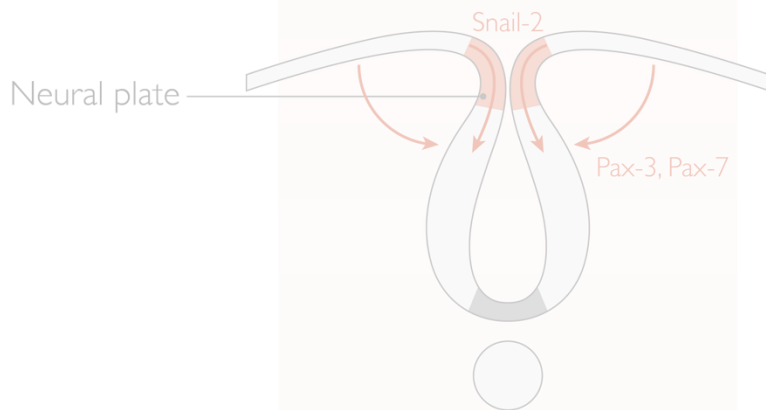
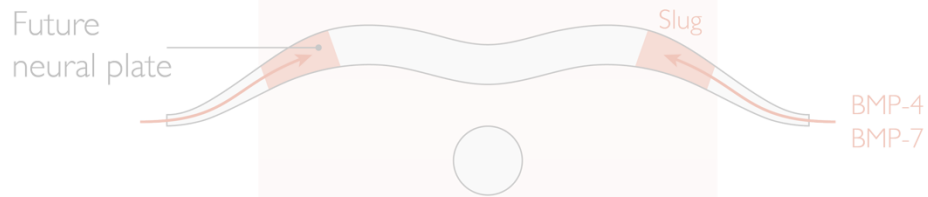
Snail-2

Pax-3, Pax-7

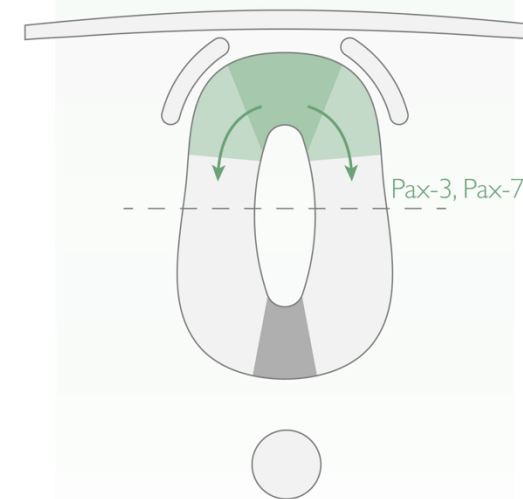
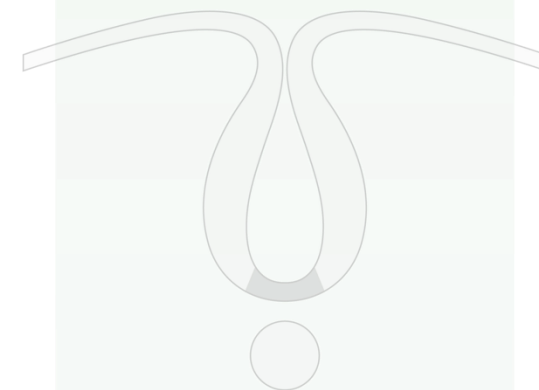
# Shh



# BMPs



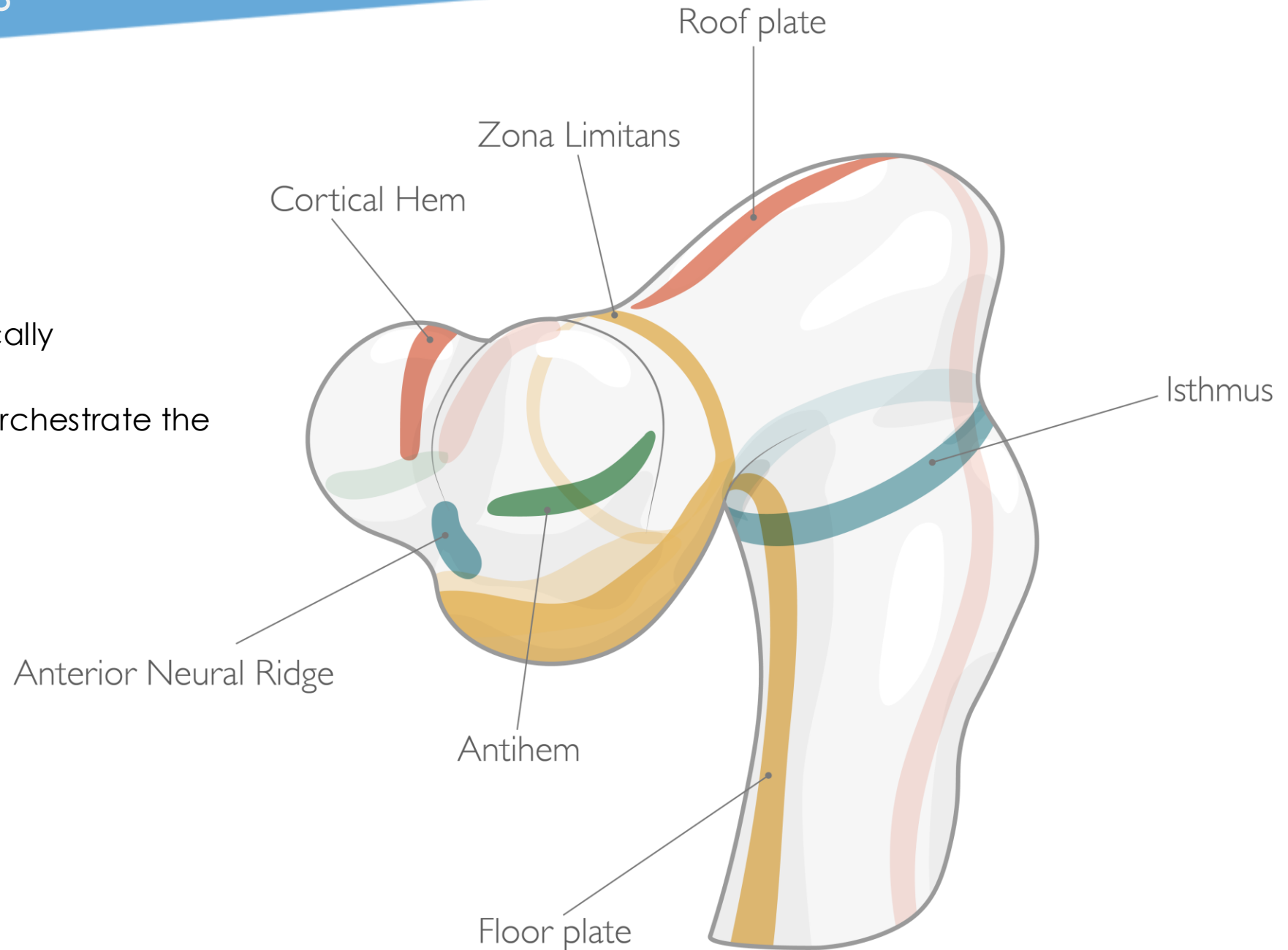
# Wnt



# Secondary organizers

## During gastrulation:

- Signals are provided extrinsically
- Specific neural progenitors orchestrate the morphogenesis of the brain

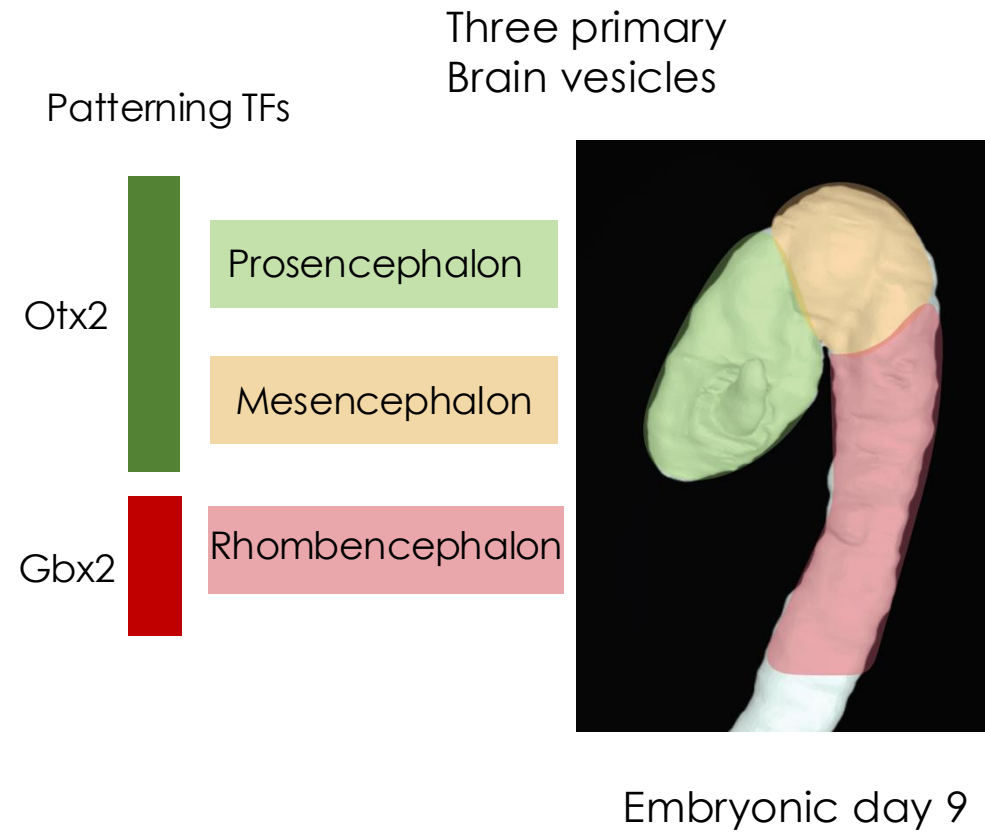


**Ventralizing (Shh) organizers**

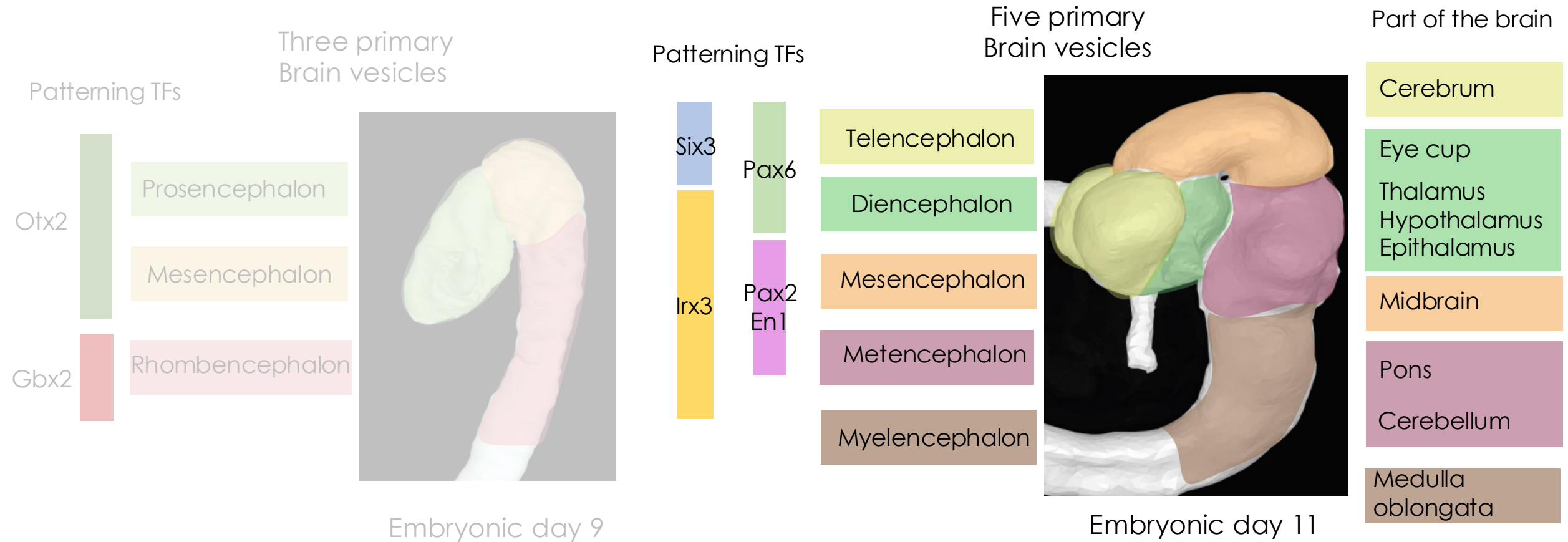
**Dorsalizing (Bmp, Wnt) organizers**

**Boundary (Fgf) organizers**

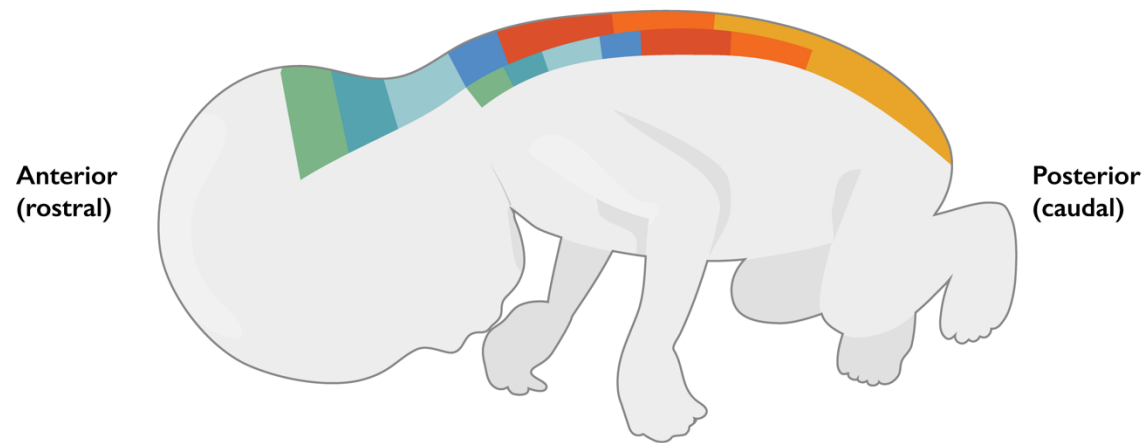
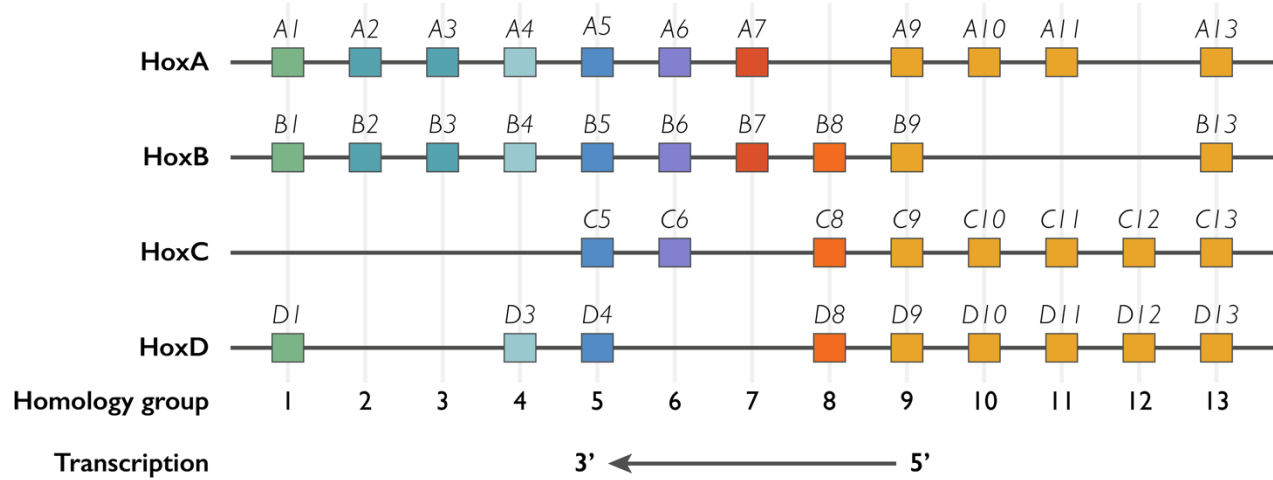
# Early regionalization



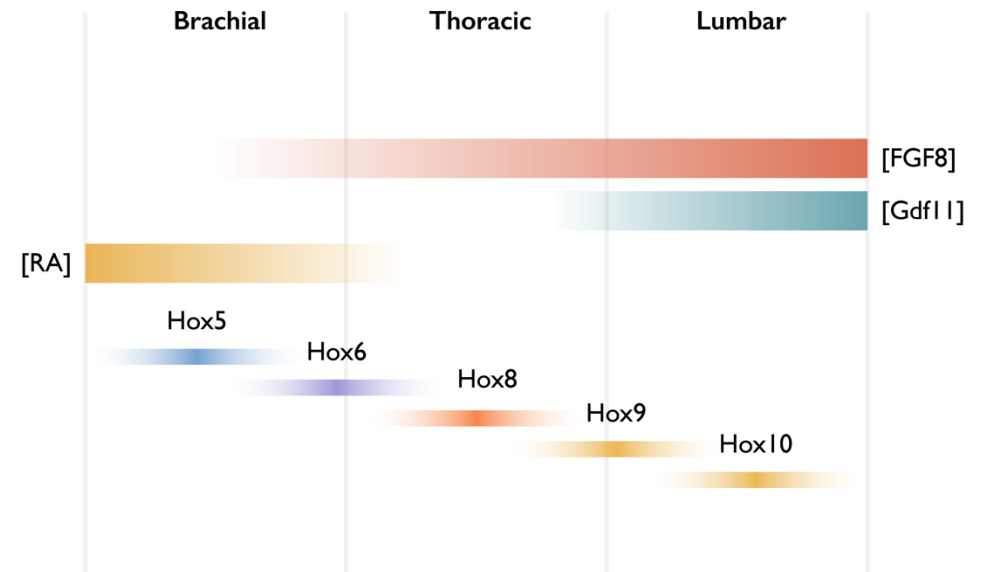
# Early regionalization



# Spinal cord



## Rostrocaudal axis

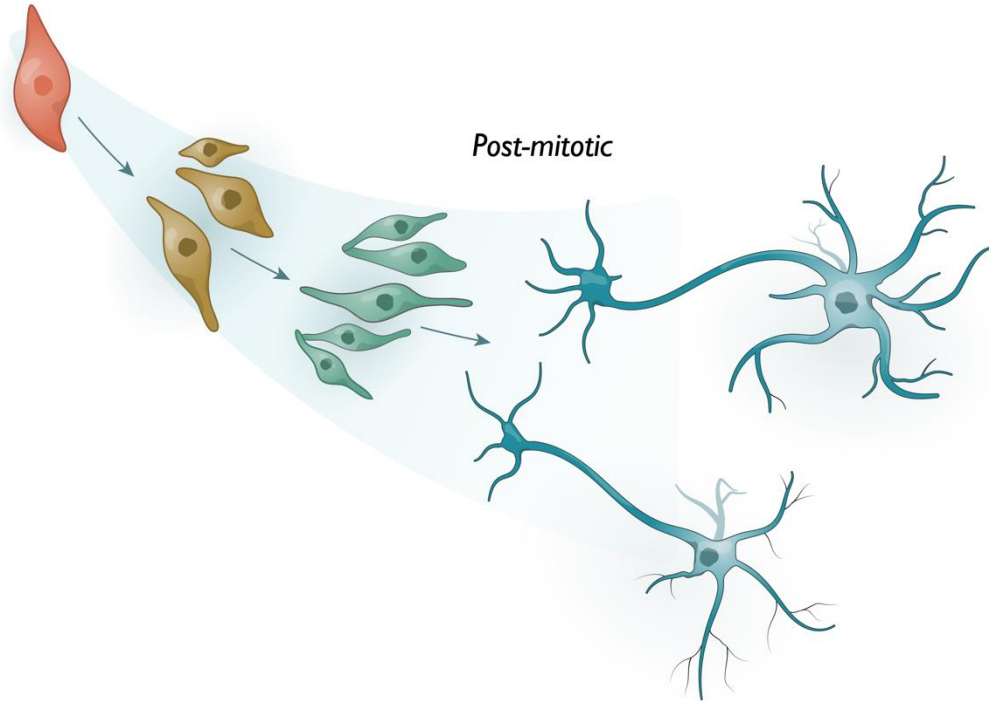




# Differentiation & migration

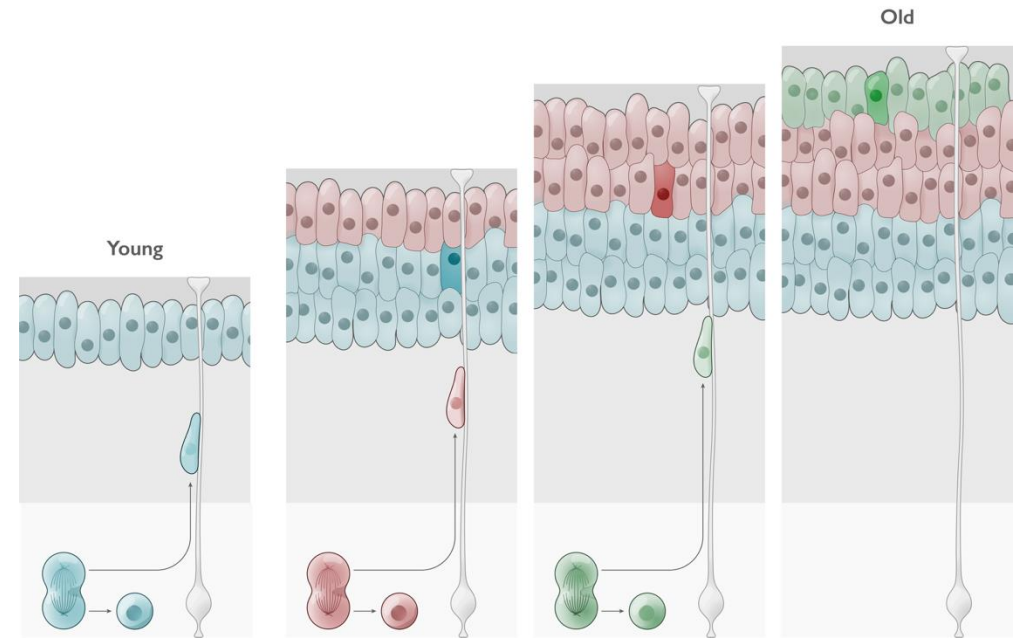
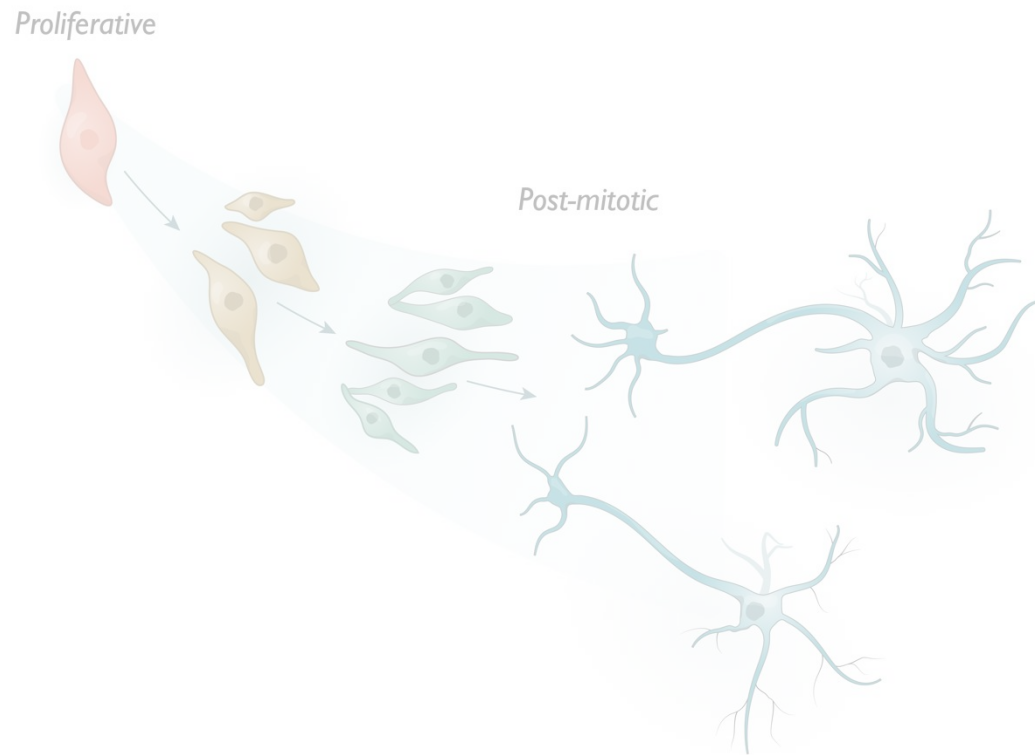
**Cellular differentiation:** acquisition of specific functions and morphology

*Proliferative*

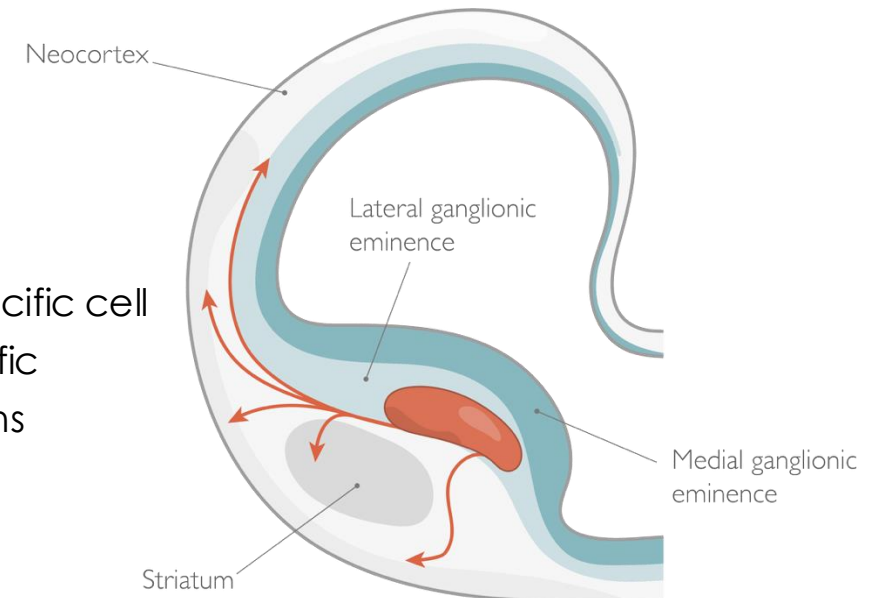


# Differentiation & migration

**Cellular differentiation:** acquisition of specific functions and morphology



**Cellular migration:** specific cell types migrate to specific layers and brain regions

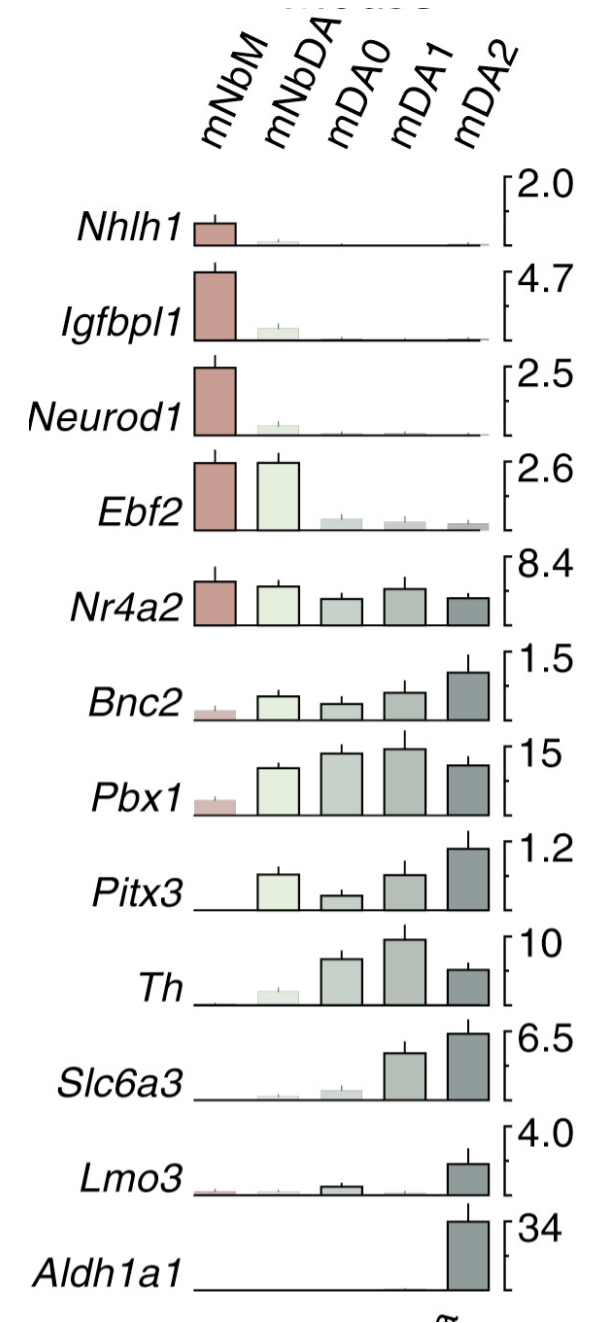
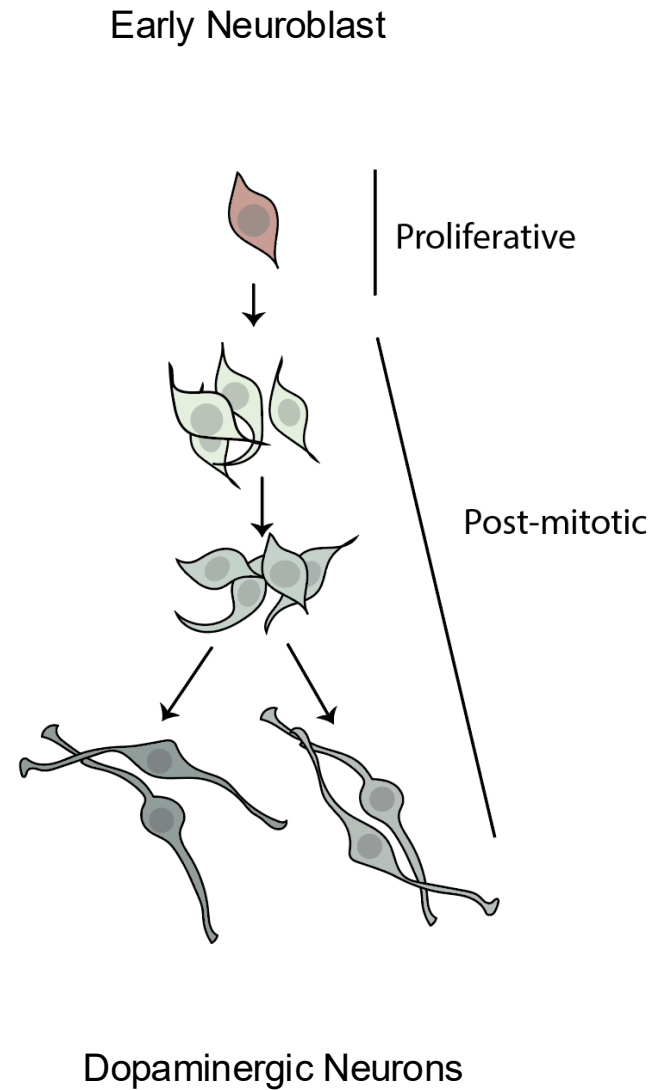


# Differentiation

Neuronal differentiation is a complex process

that leads to the acquisition of:

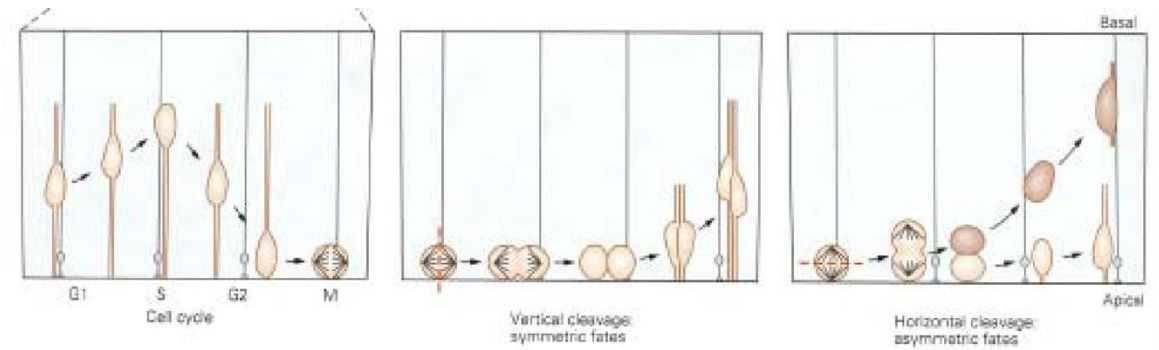
- Mature transcriptional pattern
- Neurotransmitter specificity
- Electrophysiological
- Morphological differences



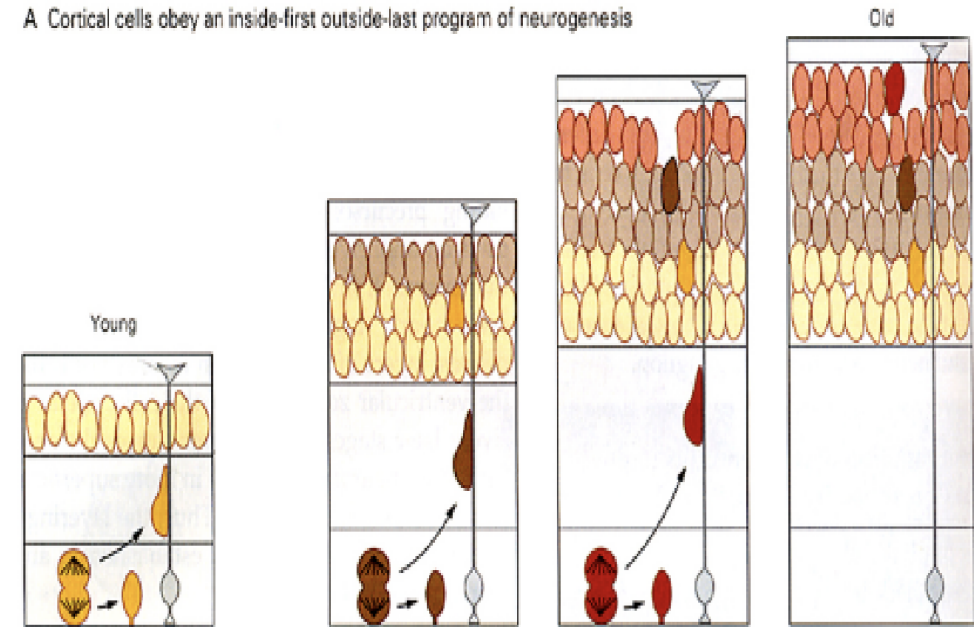
# Ventricular zone

## The ventricular zone and radial glial cells

- Interkinetic nuclear migration
- Generation in an inside-out fashion
- Histogenetic production of different types



A Cortical cells obey an inside-first outside-last program of neurogenesis



# Migration

## The migration of interneurons

- Neuroblast from the MGE migrate throughout the subpallium
- Sort out in 2 main streams towards *cortex* or the *striatum*.
- Assisted by LGE-derived cells and by motogenic and chemoattractive factors.
- Migration restriction in two streams: the SVZ and MZ

