



**UFRJ**

**UNIVERSIDADE FEDERAL  
DO RIO DE JANEIRO**



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Programa de  
Pós-Graduação em

Universidade Federal do Rio de Janeiro

PROEX CAPES nota 6

PPG Linguística desde janeiro de 1968

# LINGUÍSTICA

## Corticoneurogênese: Um século de progressos



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# LINGUÍSTICA

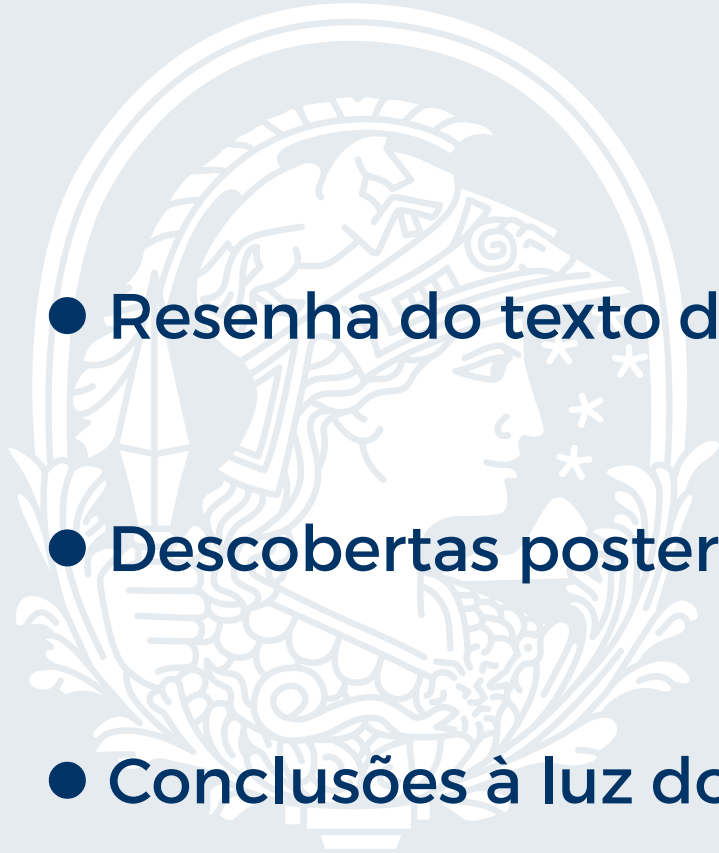
**Disciplina: Neurofisiologia da leitura**

**Docente: Aniela Improta França**

**Discente: Claudio de Alencar Padua**

# APRESENTAÇÃO

- Resenha do texto de Rakic – descobertas históricas
- Descobertas posteriores – novos métodos
- Conclusões à luz dos novos descobrimentos



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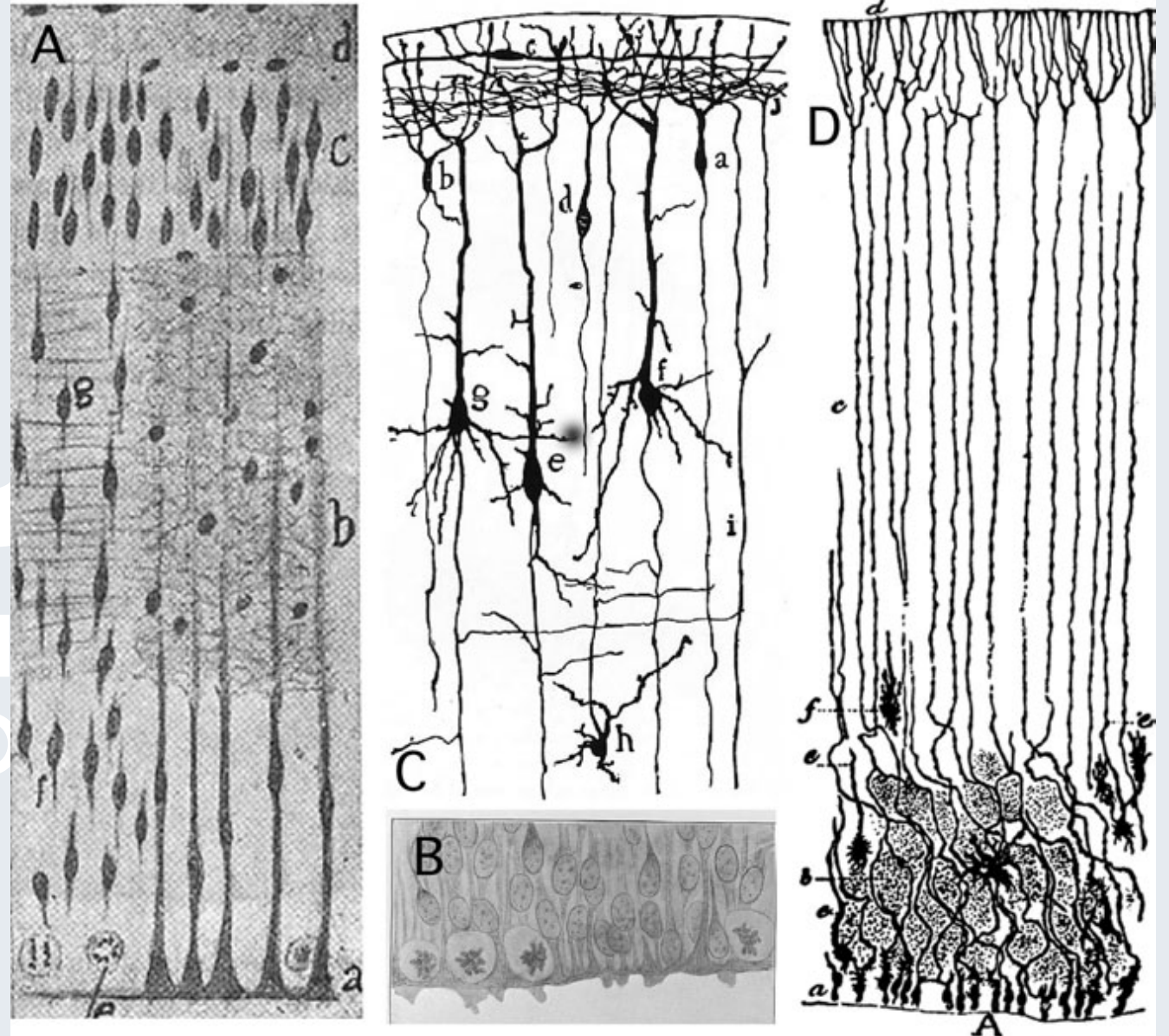


# **A Century of Progress in Corticoneurogenesis: From Silver Impregnation to Genetic Engineering**

UNIVERSIDADE FEDERAL  
**Pasko Rakic, 2006**  
BONFIM DE SANEIRO

# Descobertas iniciais

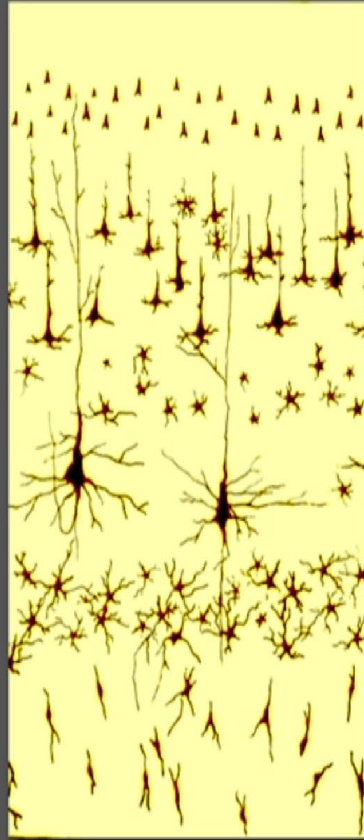
Métodos clássicos de  
marcação histológica  
(Wilhelm His, 1874)



# Descobertas iniciais

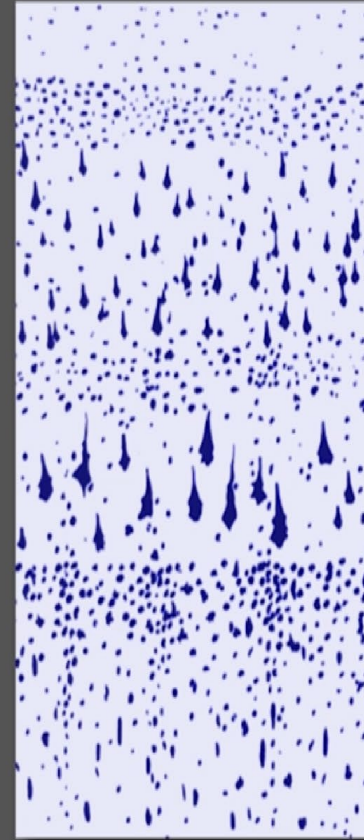


**ALL INFORMATION**



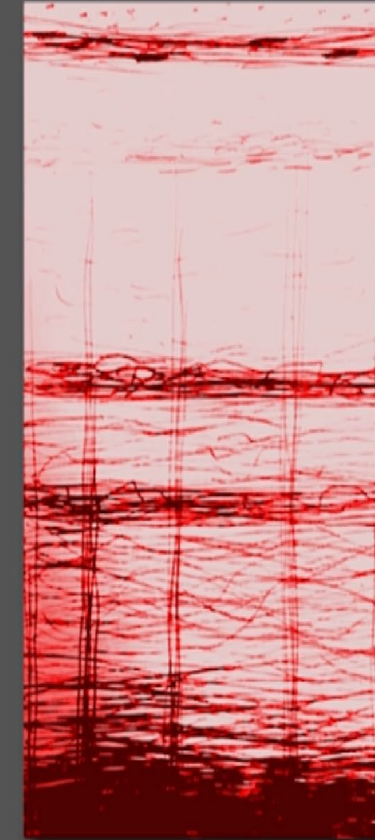
**GOLGI STAIN**

LIMITED NUMBER OF  
CELLS SEEN IN THEIR  
ENTIRETY



**NISSL STAIN**

STAINS ROUGH ER SO  
SHOWS CELL BODIES  
AND PROXIMAL  
DENDRITES



**WEIGERT STAIN**

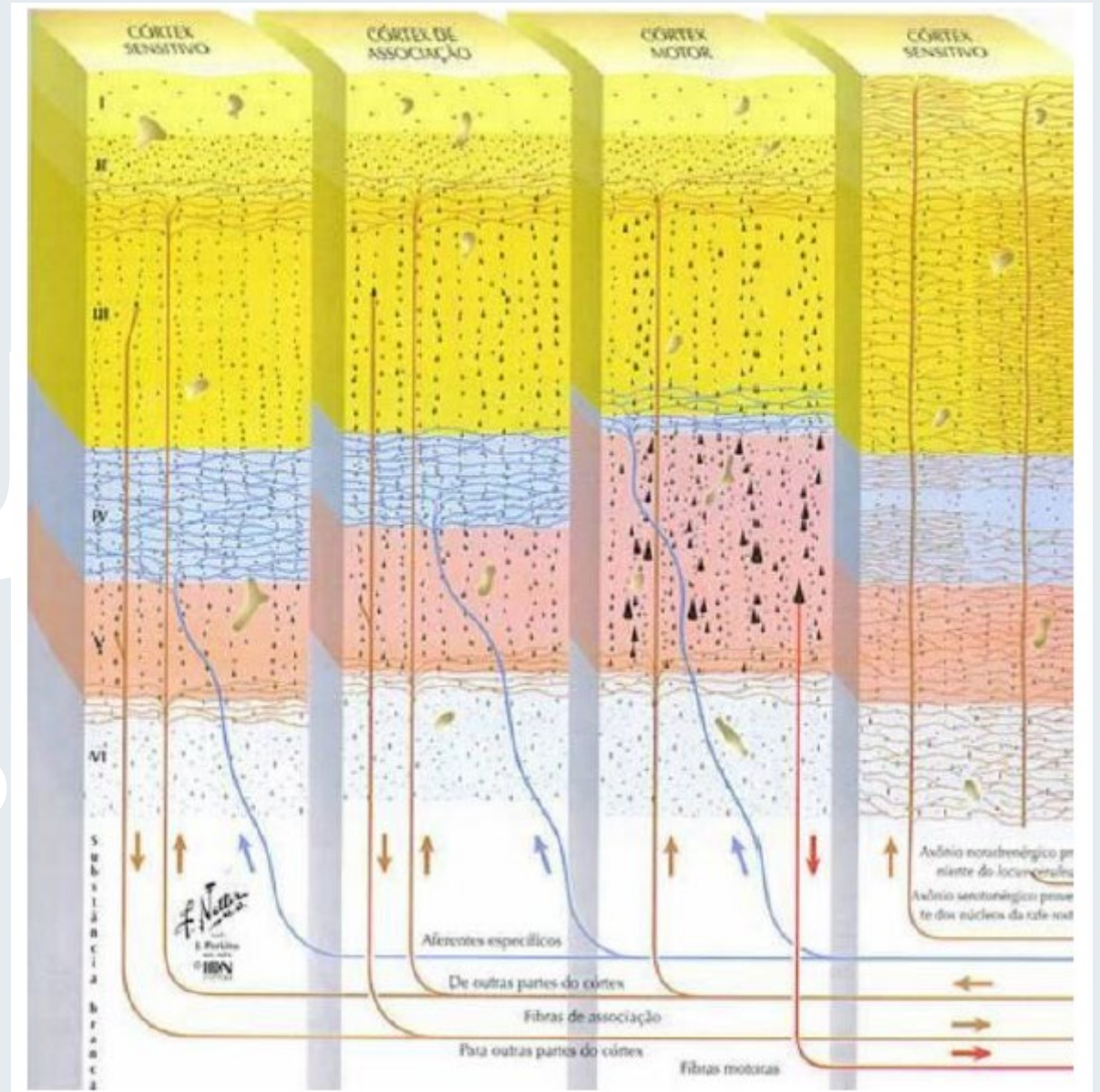
MYELINATED FIBERS  
SO SHOWS AXONAL  
DISTRIBUTION

# Descobertas iniciais

Mapa de Korbinian  
Brodmann das áreas corticais  
em humanos (1909)



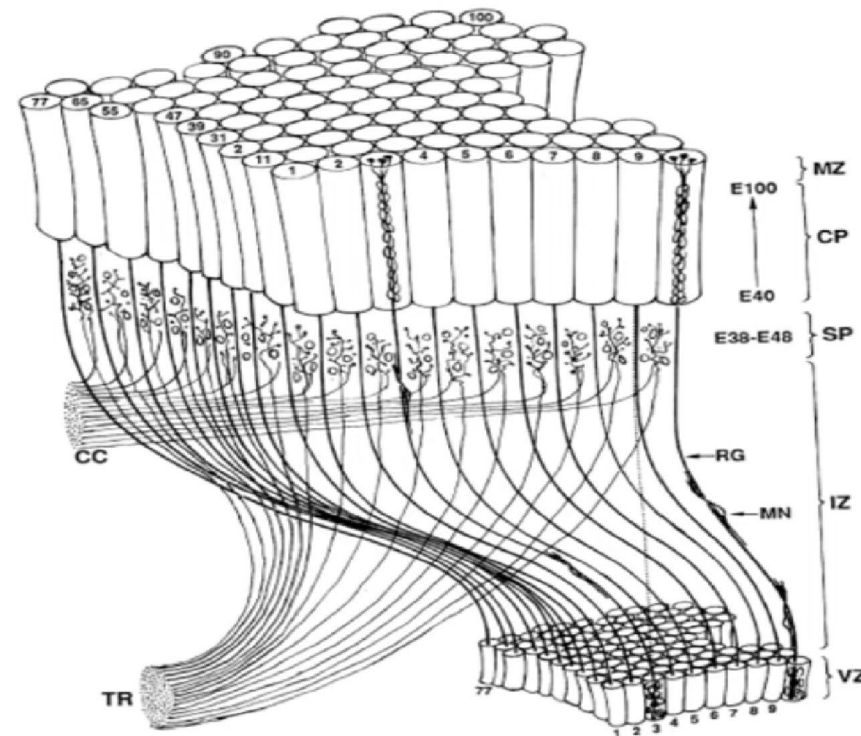
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# Citoarquitetura Cortical

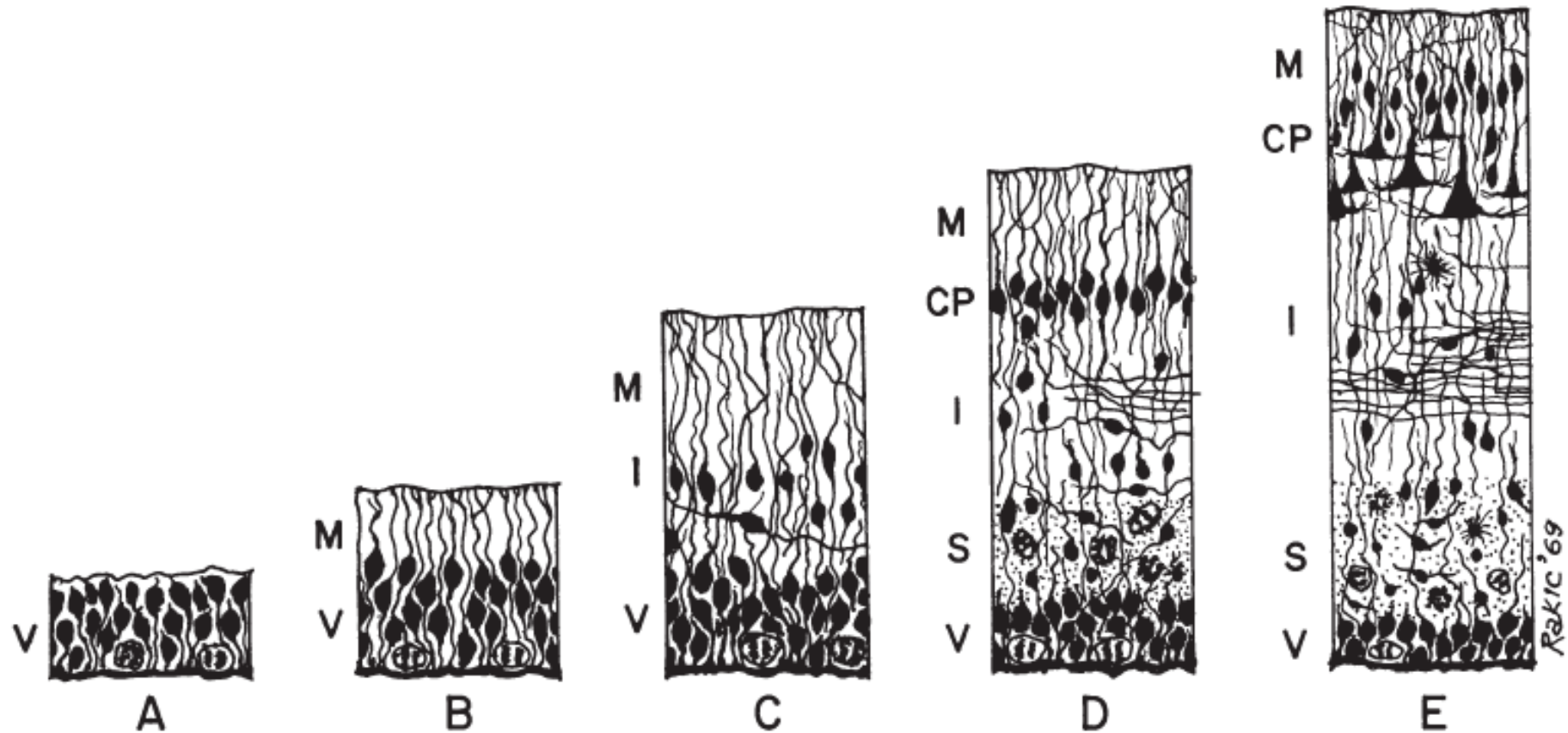
## The Radial Unit Hypothesis: A continuous radial glial scaffold



Rakic, P. (1988) Science

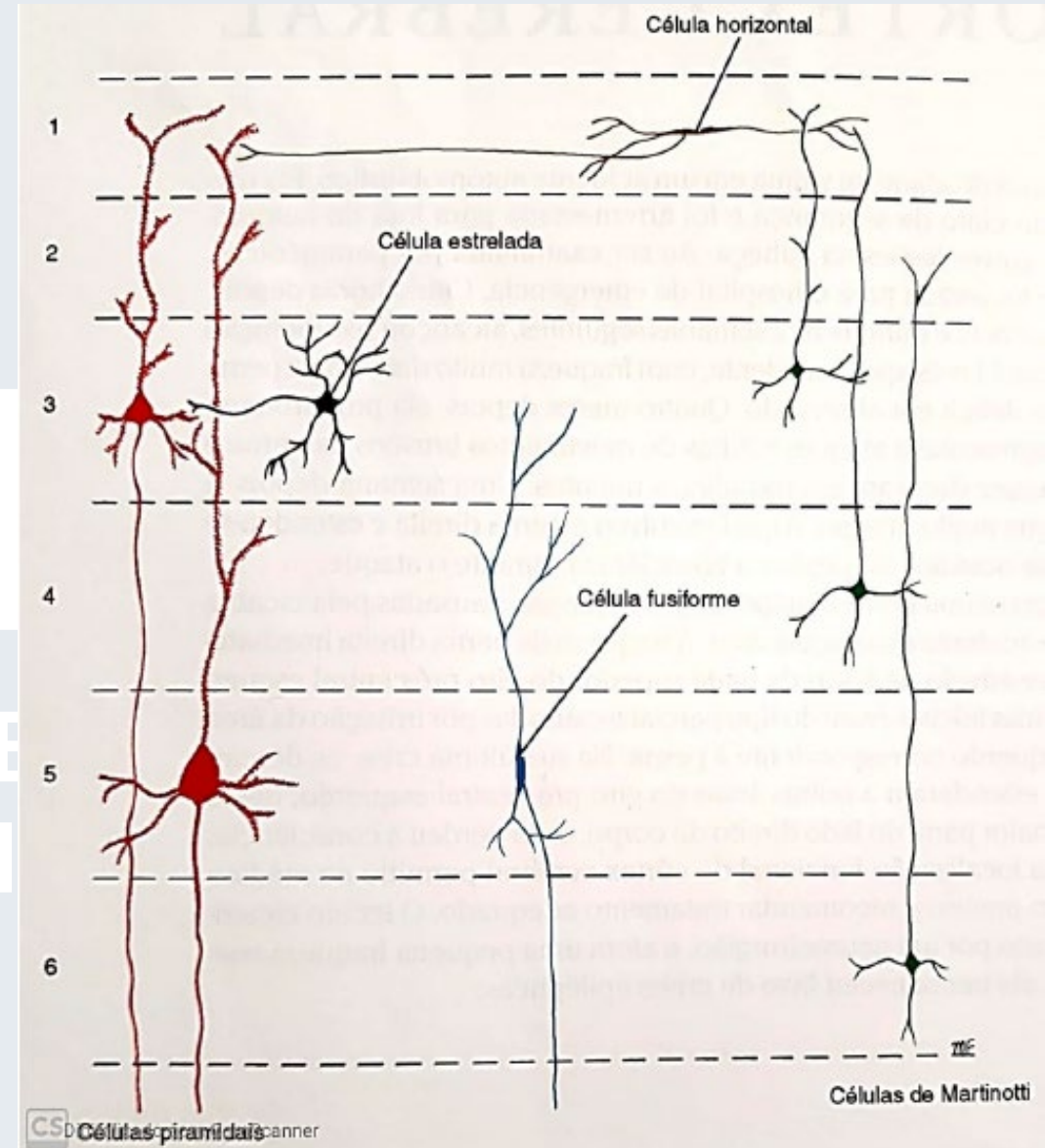
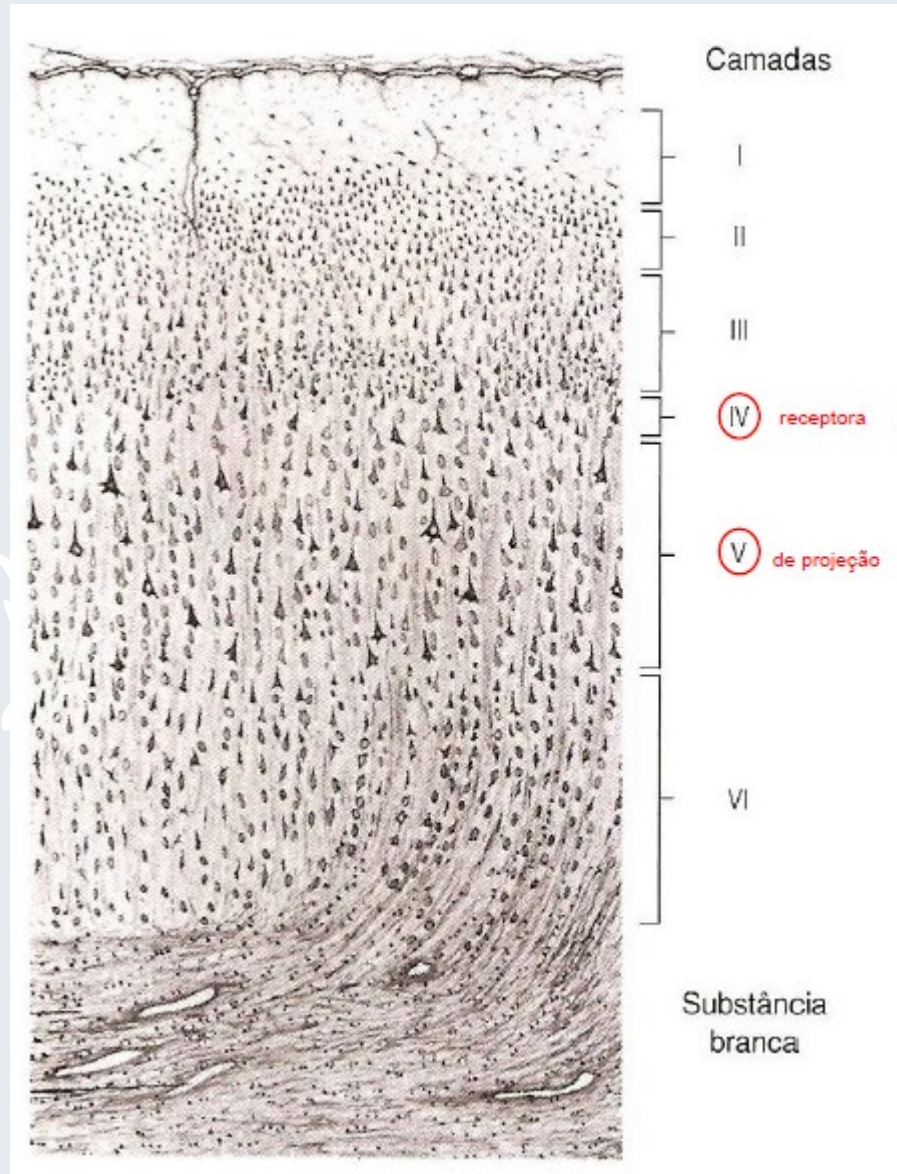
Hipótese da unidade radial: um “andaime” radial contínuo de glia

# Citoarquitetura Cortical

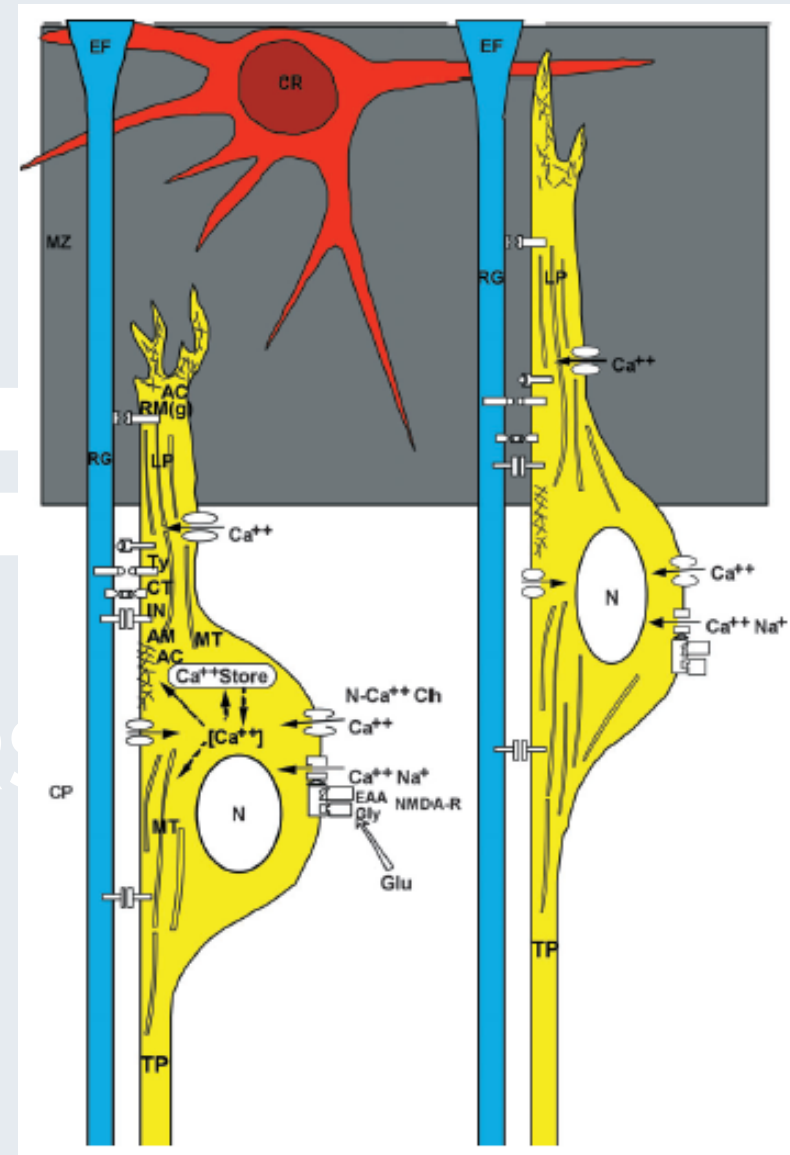
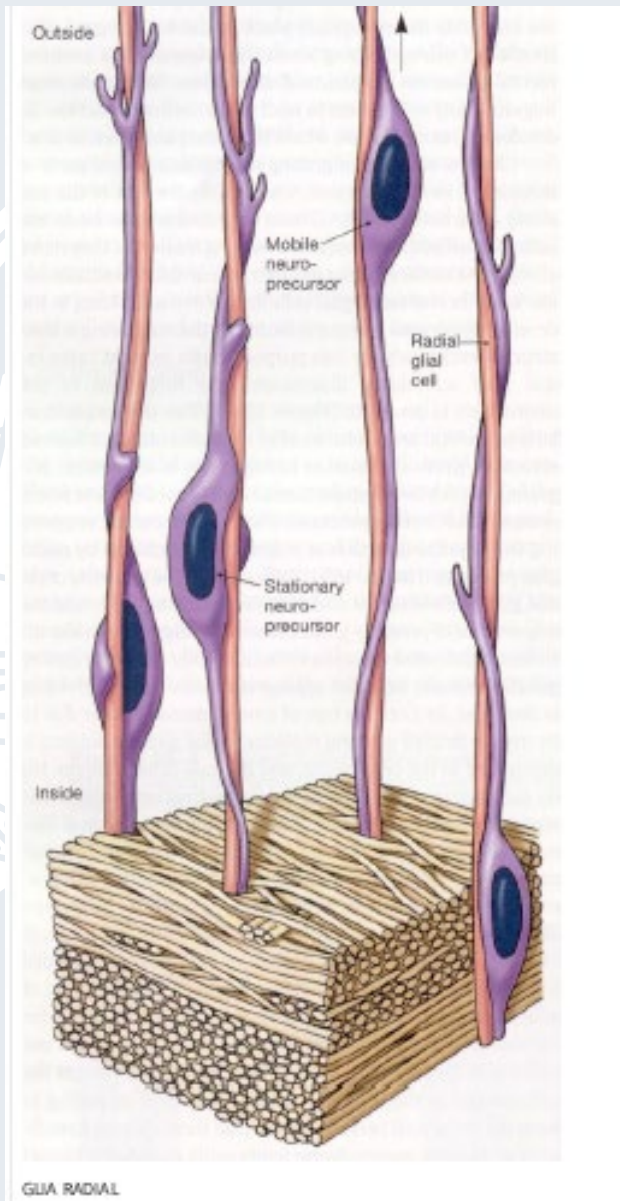


Esquema proposto por Rakic (1969) – Tese doutoral: “Studies on the proliferation, migration, and differentiation of neuroblasts during neurohistogenesis in mammals, particularly man”

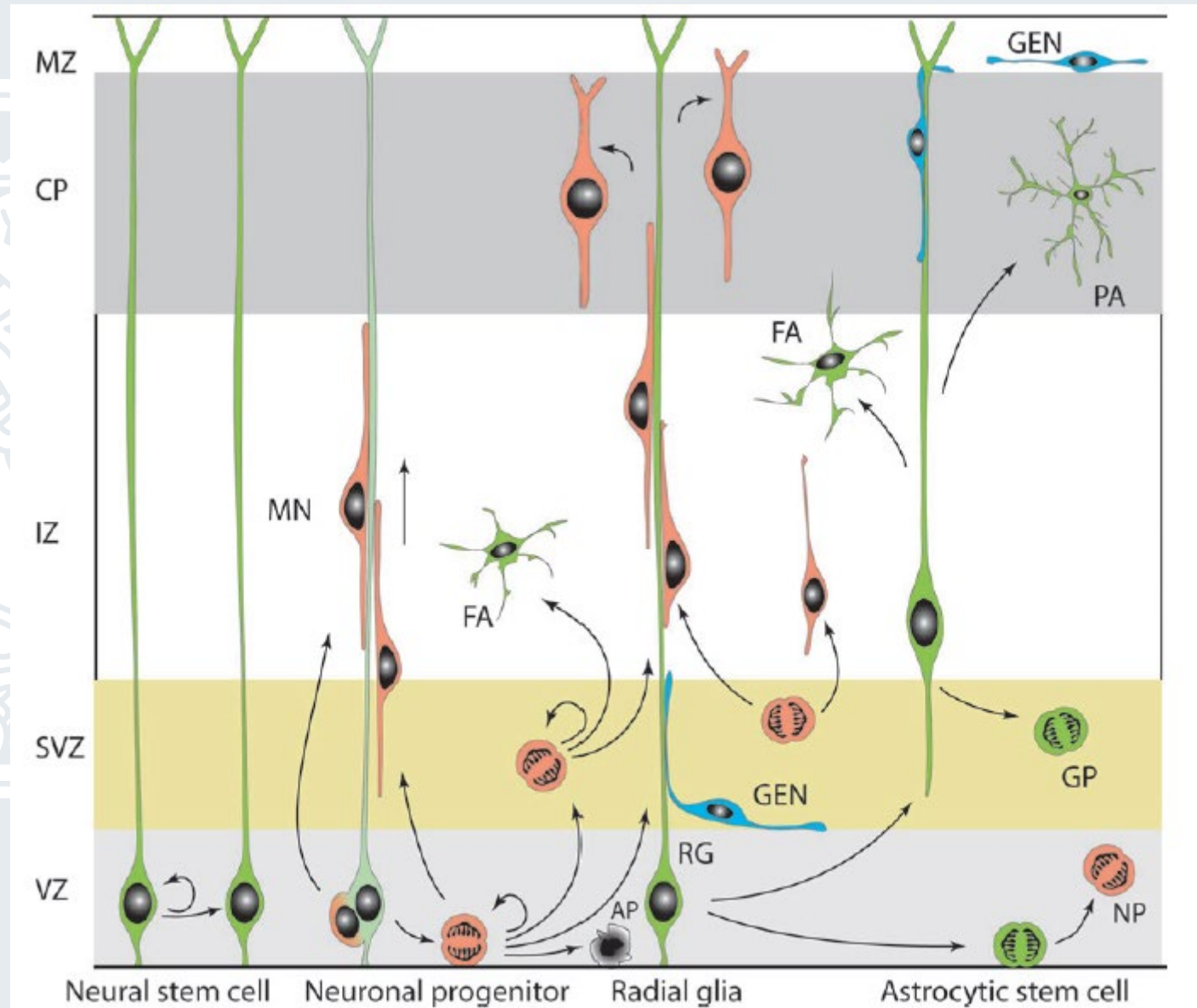
# Citoarquitetura Cortical



# Corticoneurogênese e Migração



# Corticoneurogênese e Migração



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O

# Corticoneurogênese e Migração

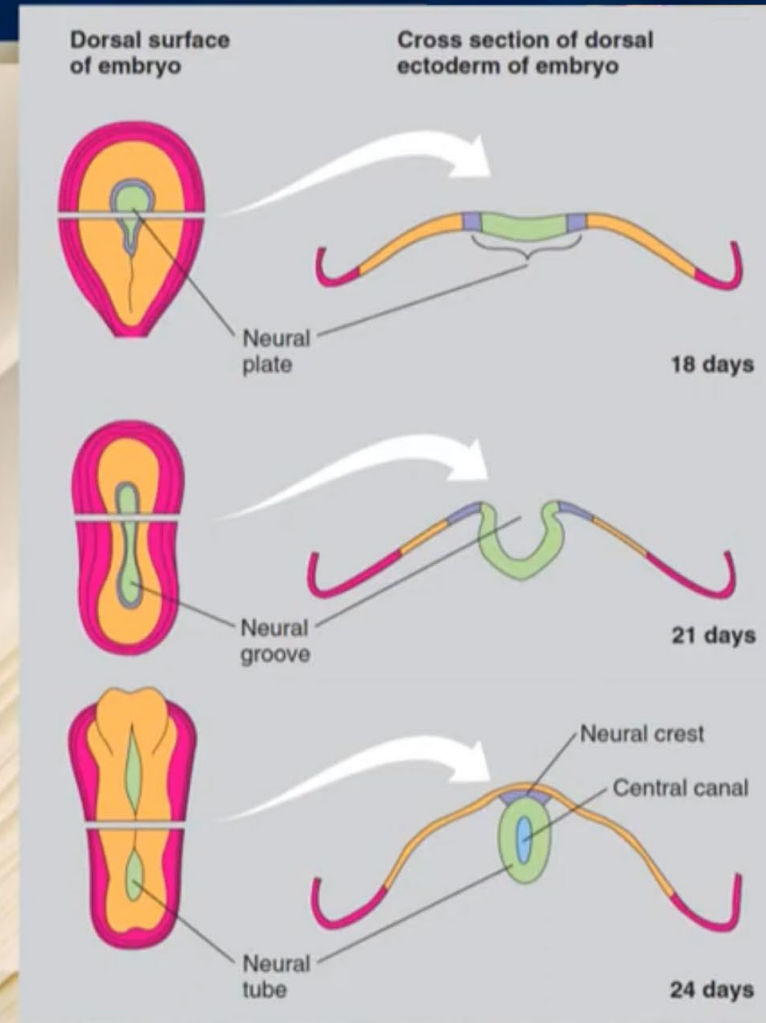
## Neural Crest

A structure dorsal to the neural tube and formed from neural tube cells  
Neural crest cells develop into the cells of the peripheral nervous system

Cells migrate long distances

Migrating neurons are guided by numerous chemicals that either attract or repel them.

Brain cannot function normally unless each class of developing neurons arrives at the correct location.



RAL

# Corticoneurogênese e Migração

## Migration

Two types of neural tube migration

Radial migration (moving out)

Tangential migration (moving up)

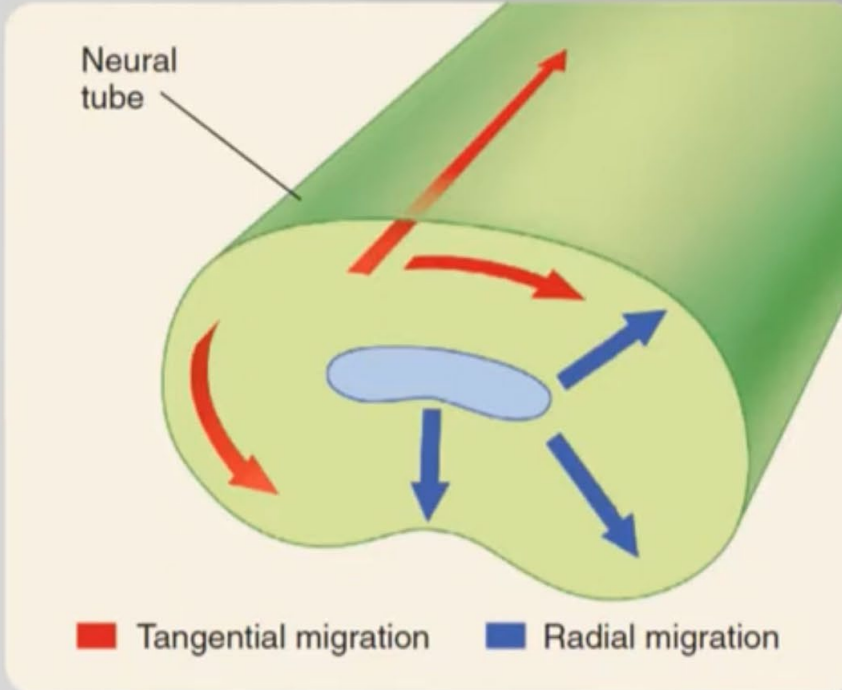
Two methods of migration

**Somal Translocation**– an extension develops in the direction of the migration, cell body follows

**Glial-mediated migration** – cell moves along a radial glial network

Most cells engage in both types of migration

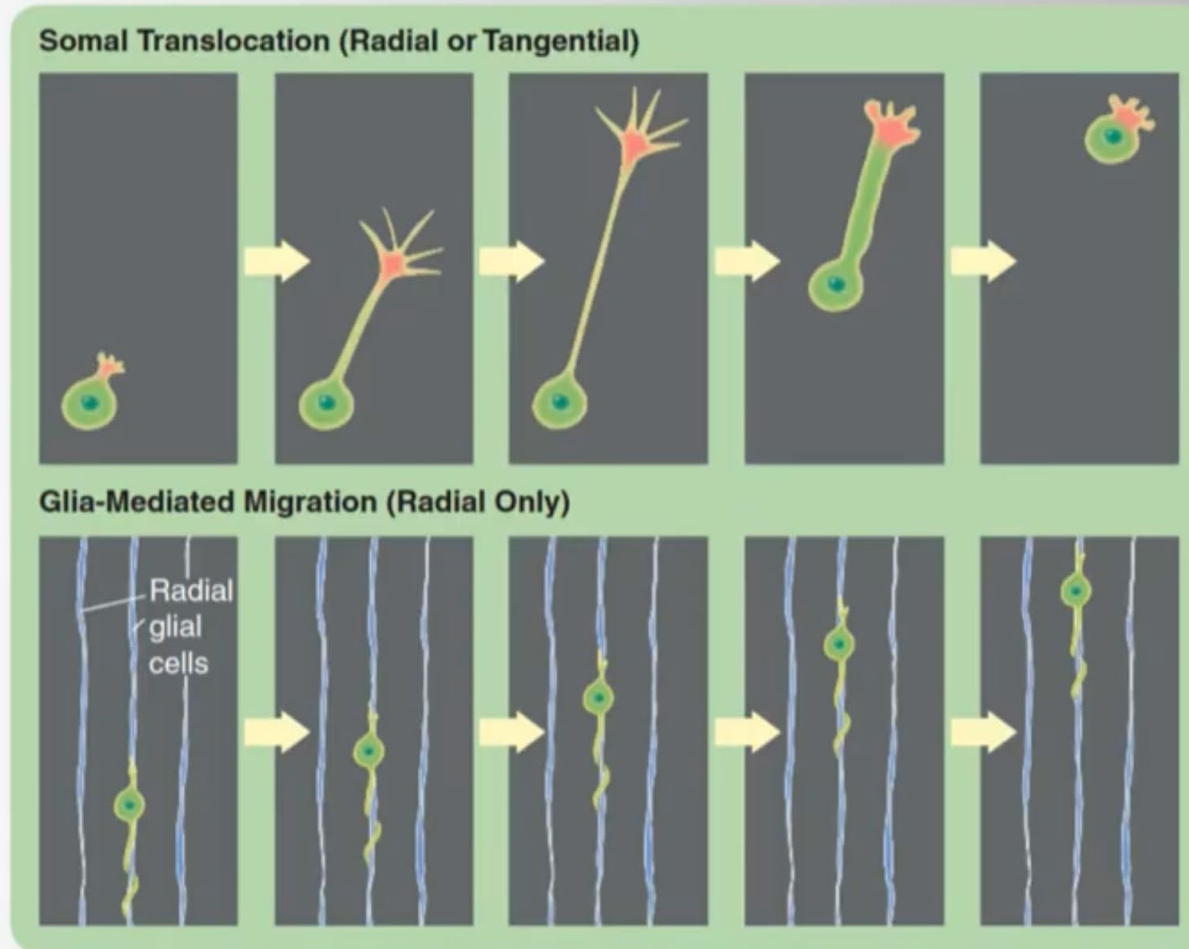
Many radial glial cells eventually develop into neurons



RAL

# Corticoneurogênese e Migração

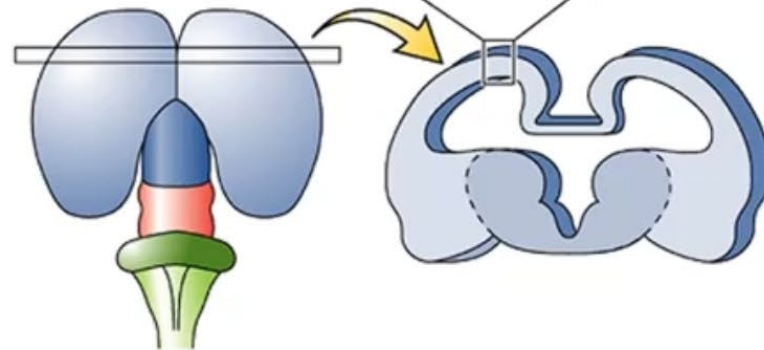
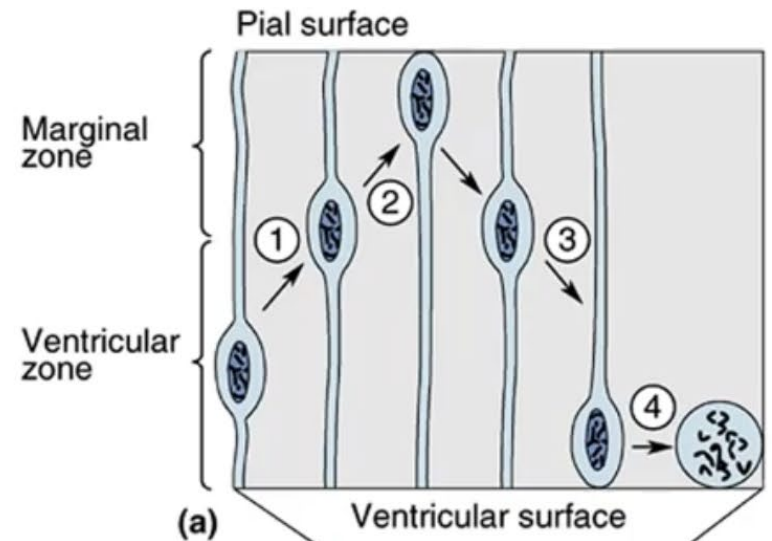
## Migration



RAL



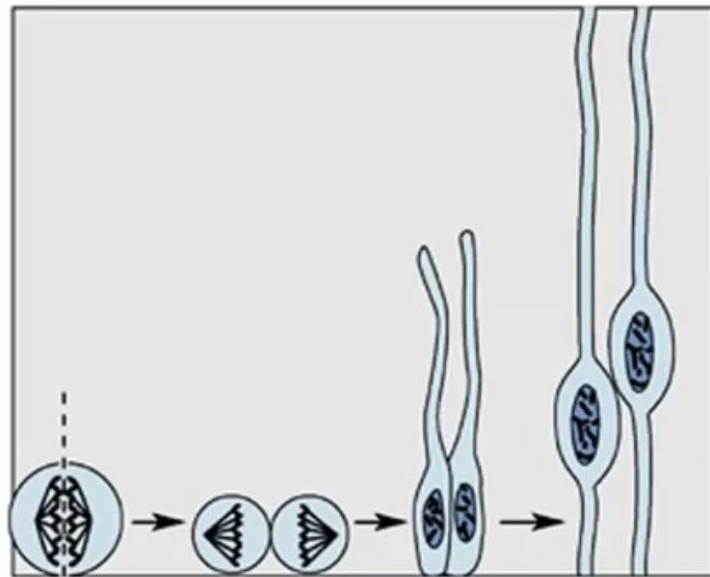
# Corticoneurogênese e Migração



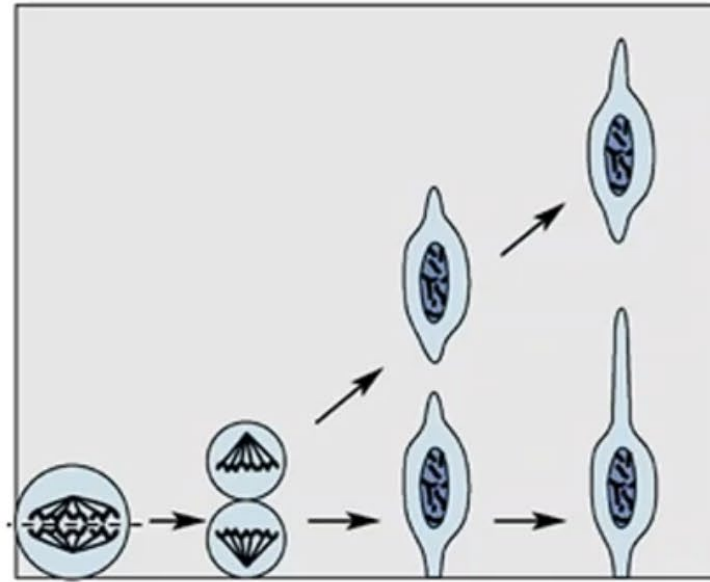
## Neurogenesis

**Neural stem cells** divide in the **ventricular zone**

# Corticoneurogênese e Migração



(b) Vertical cleavage



(c) Horizontal cleavage

## Neurogenesis

**Neural stem cells** divide in the **ventricular zone**

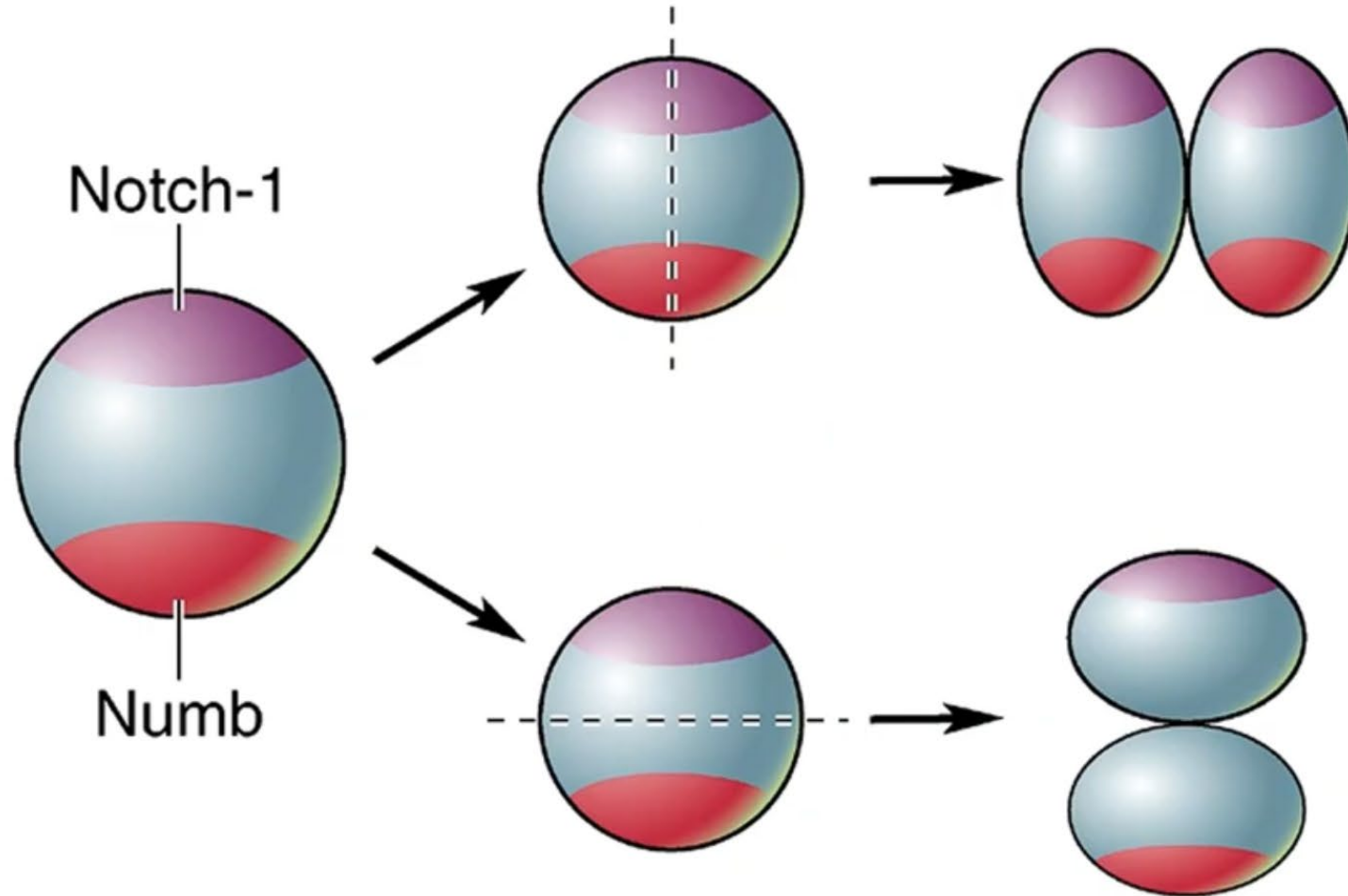
vertical cleavage

- both daughter cells turn back into stem cells

horizontal cleavage

- cell on ventricular side turns back into stem cell
- cell on pial side turns into mature neuron or glia

# Corticoneurogênese e Migração



## Neurogenesis

**Neural stem cells** divide in the **ventricular zone**

vertical cleavage

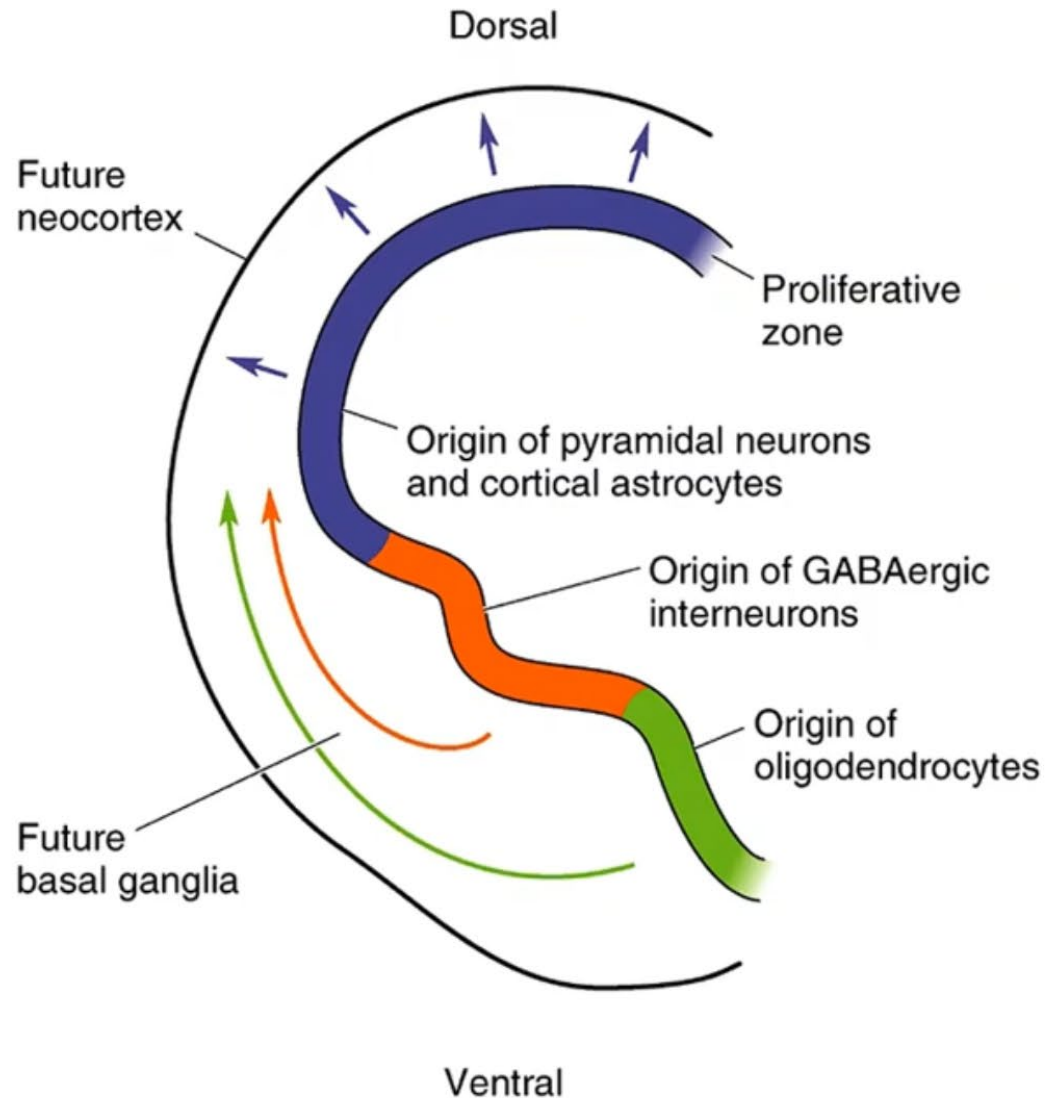
- both daughter cells turn back into stem cells

horizontal cleavage

- cell on ventricular side turns back into stem cell
- cell on pial side turns into mature neuron or glia

intracellular signals determine cell fate

# Corticoneurogênese e Migração



## Cell migration

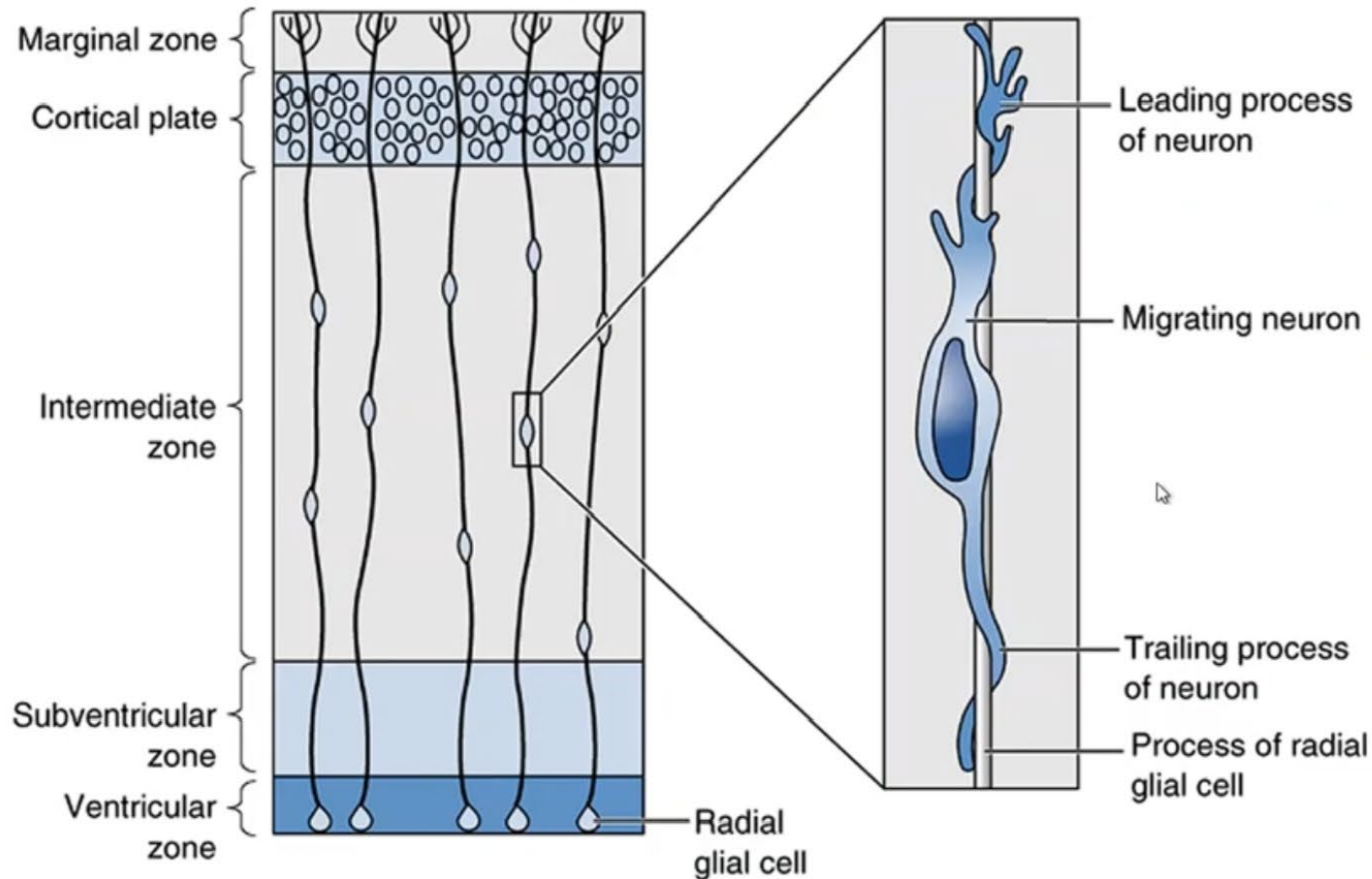
### Radial migration

- pyramidal neurons
- cortical astrocytes

### Tangential migration

- cortical interneurons
- oligodendrocytes

# Corticoneurogênese e Migração



## Cell migration

### Radial migration

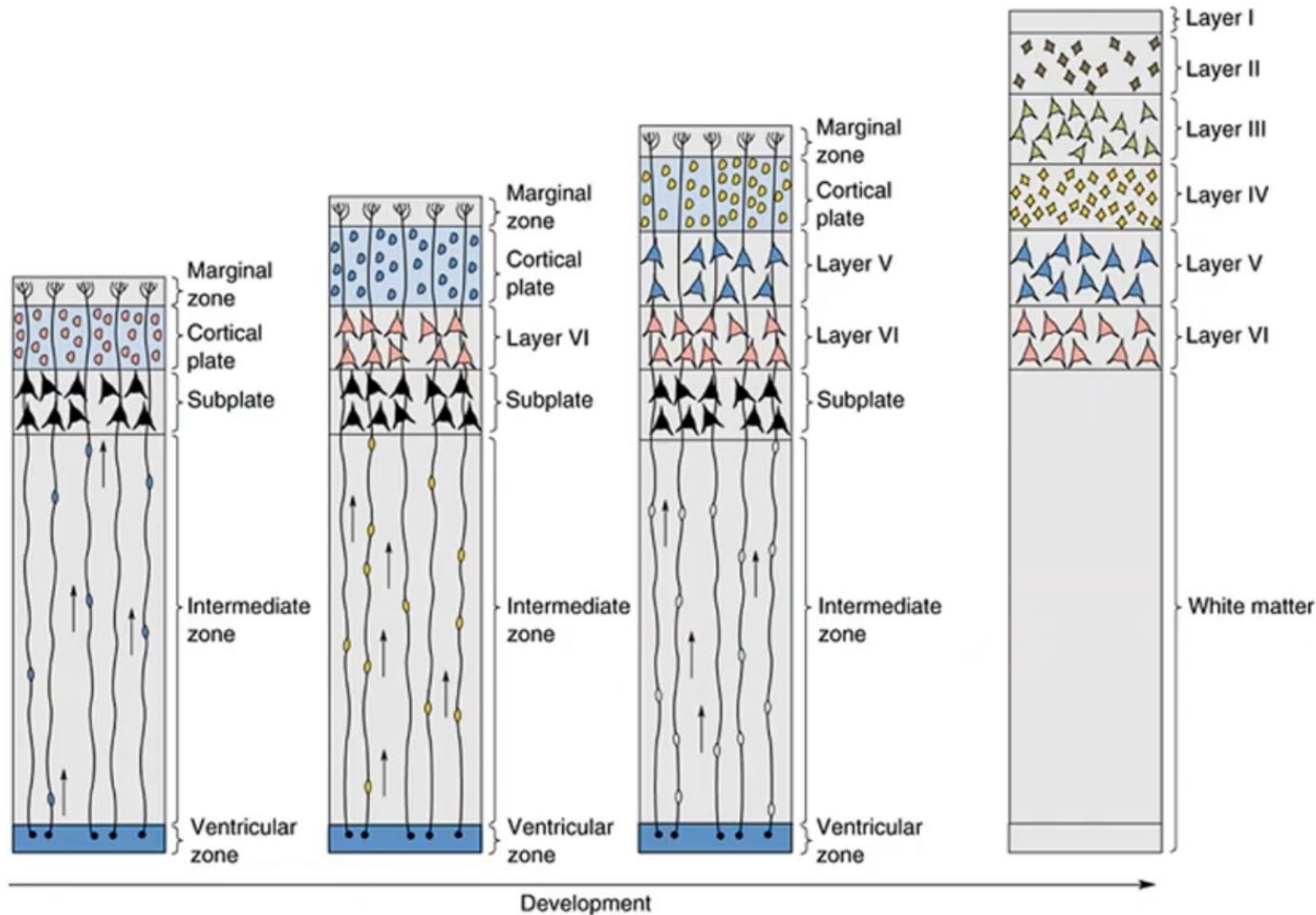
- pyramidal neurons
- cortical astrocytes

### Tangential migration

- cortical interneurons
- oligodendrocytes

Radial glial cells guide migrating neurons

# Corticoneurogênese e Migração



## Cell migration

### Radial migration

- pyramidal neurons
- cortical astrocytes

### Tangential migration

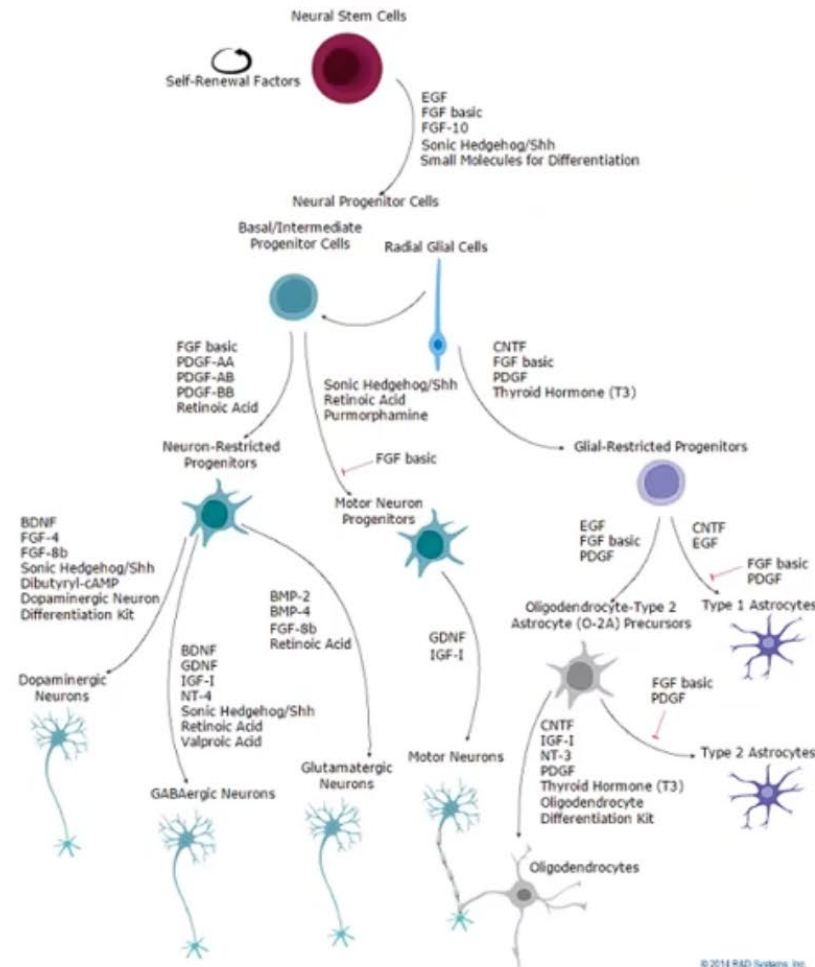
- cortical interneurons
- oligodendrocytes

Radial glial cells guide migrating neurons

cortical layers develop "inside out" (layer VI first, layer I last)

# Corticoneurogênese e Migração

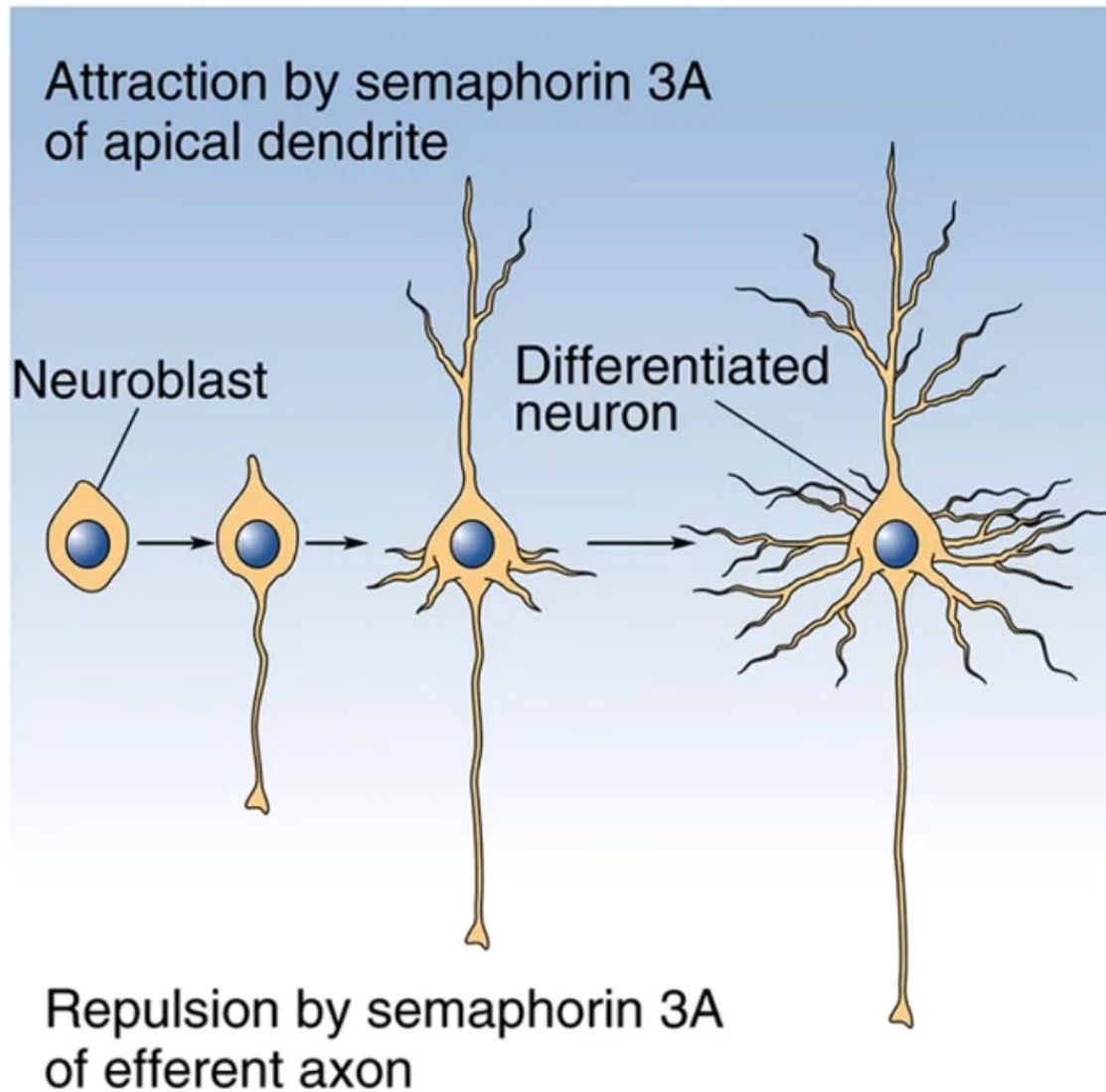
Neural Stem Cell Differentiation Pathways & Lineage-specific Markers



## Cell Differentiation

Intrinsic and extrinsic factors signal stem cells to transform into mature neurons or glia

# Corticoneurogênese e Migração



## Cell Differentiation

Intrinsic and extrinsic factors signal stem cells to transform into mature neurons or glia



# Corticoneurogênese e Migração

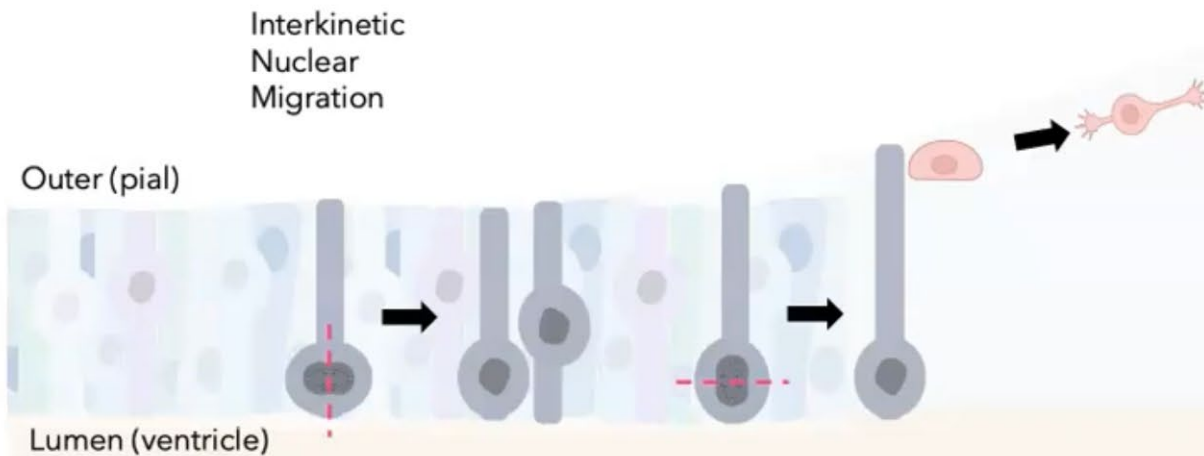
## Uma questão evolutiva

Em comparação com os demais mamíferos, o córtex dos primatas difere não apenas em complexidade, como em termos de quantidade de tipos de neurônios, diversidade de tipos de células precursoras, mas também na diversidade de tipos de neurônios que as precursoras produzem.

Arnold Kriegstein (UCSF) : Outer Subventricular Zone Radial Glia Cells  
- Brain Development

<https://www.youtube.com/watch?v=9mCBjA8wxrl&t=552s>

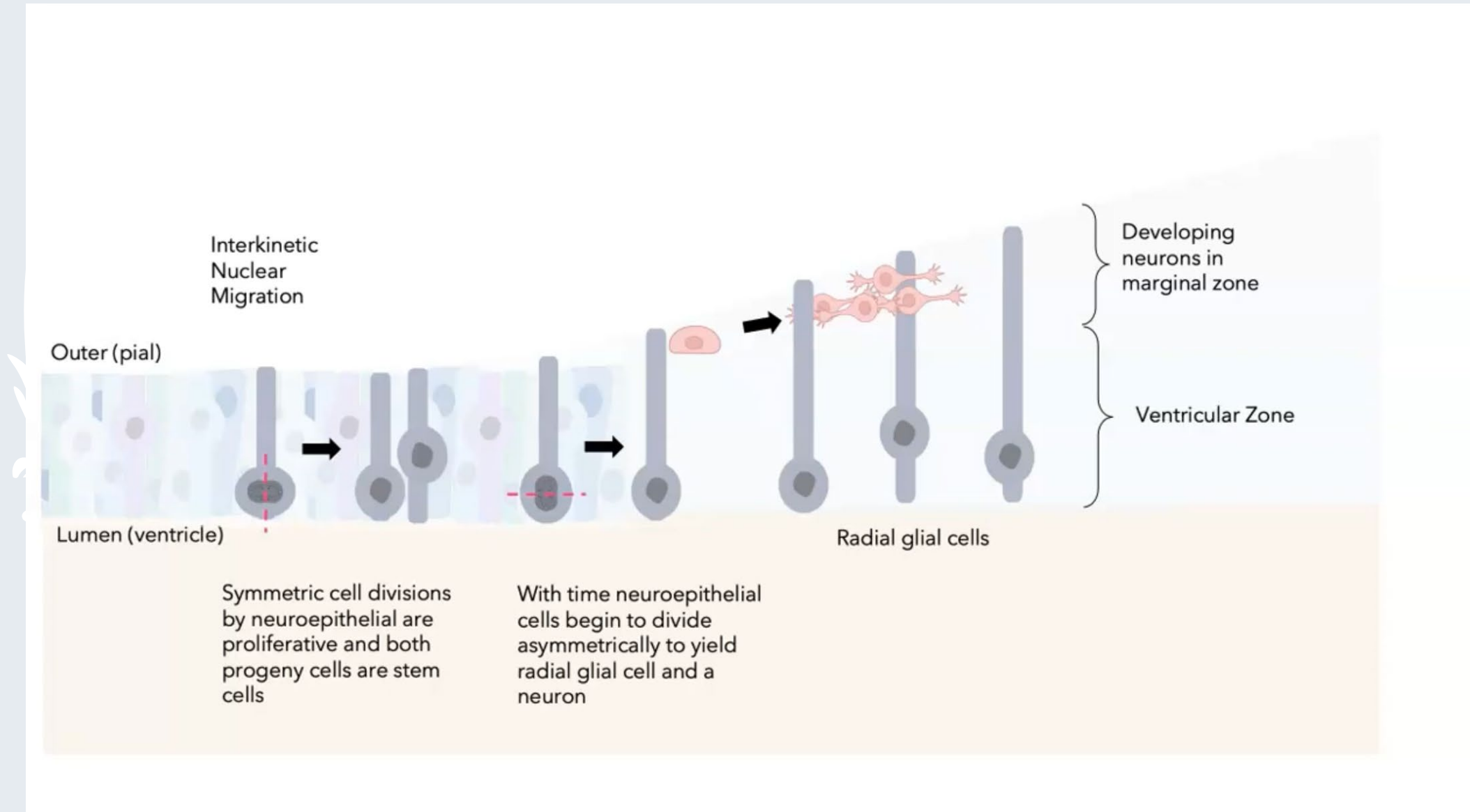
# Corticoneurogênese e Migração



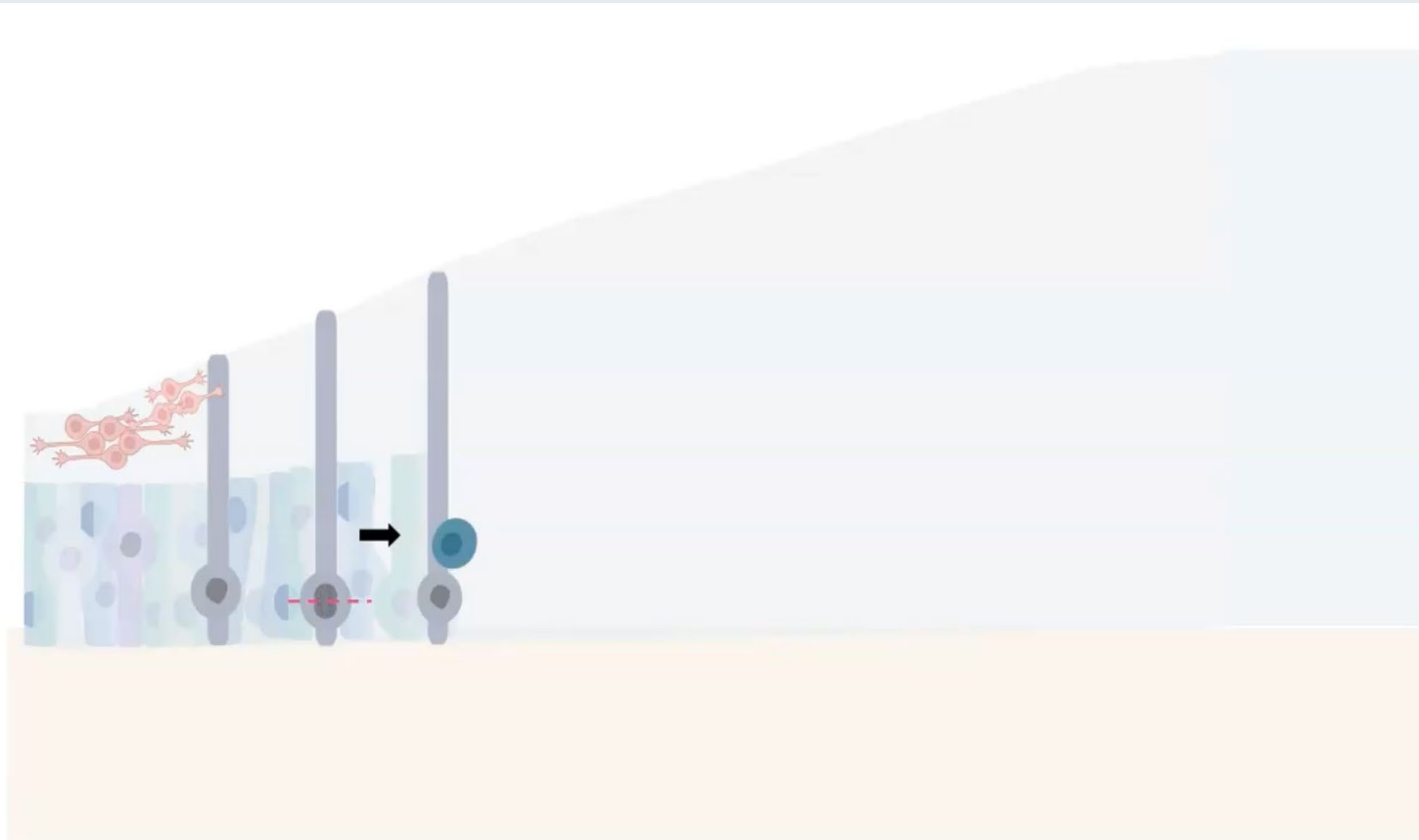
Symmetric cell divisions by neuroepithelial are proliferative and both progeny cells are stem cells

With time neuroepithelial cells begin to divide asymmetrically to yield radial glial cell and a neuron

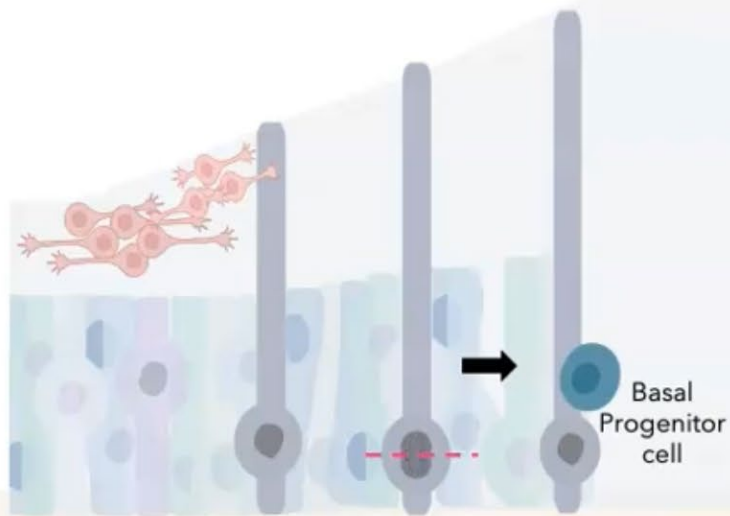
# Corticoneurogênese e Migração



# Corticoneurogênese e Migração



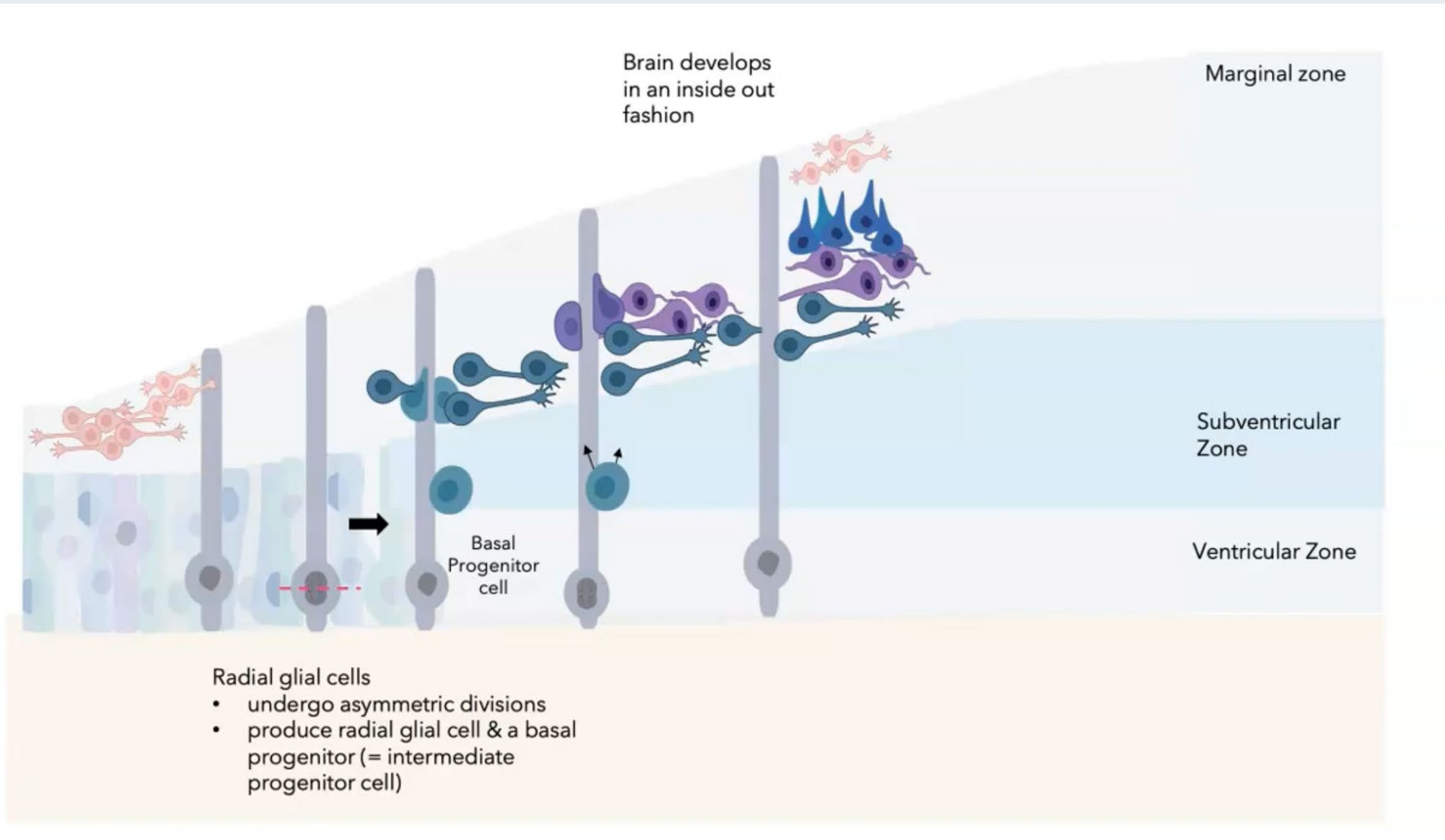
# Corticoneurogênese e Migração



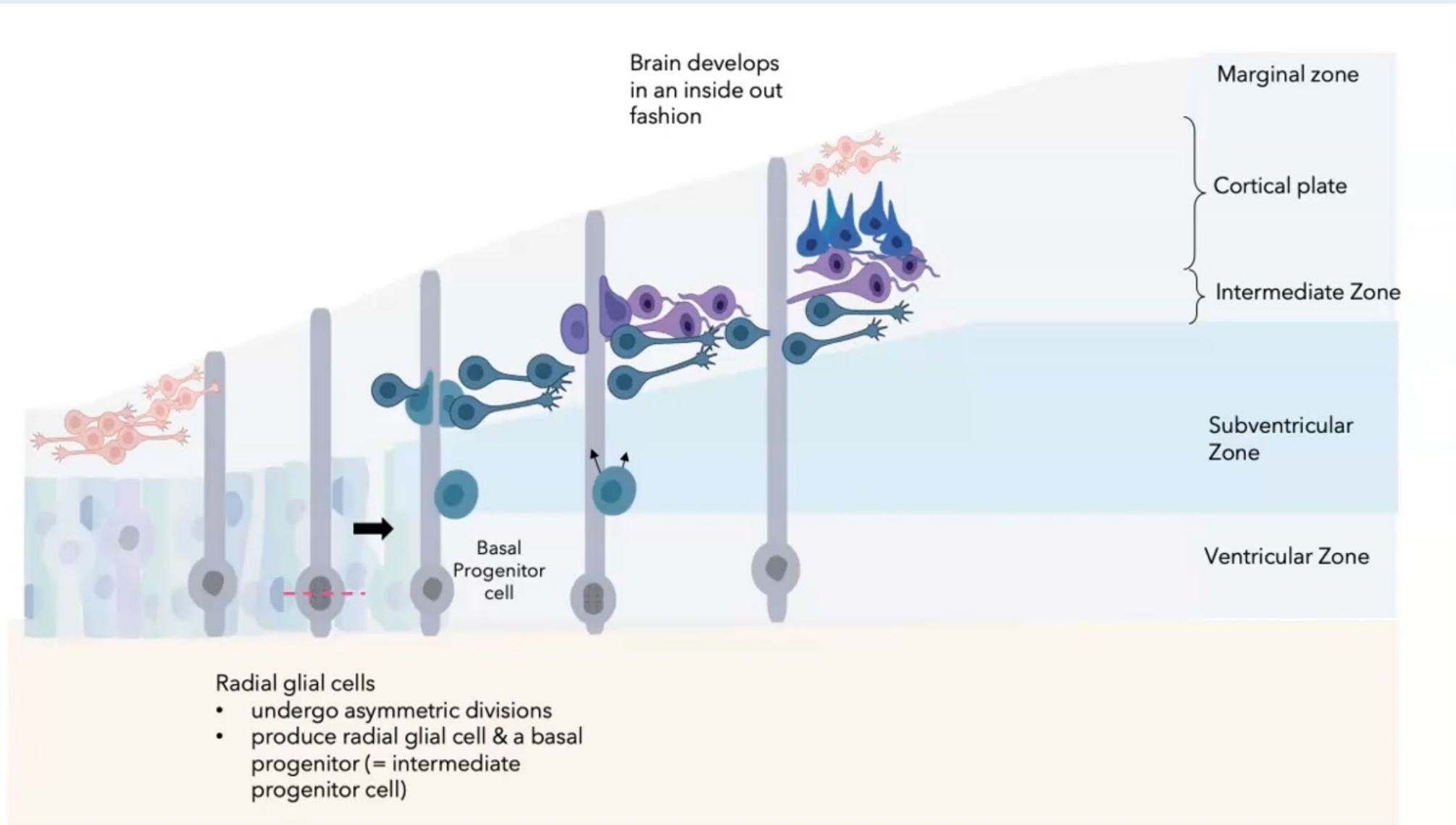
Radial glial cells

- undergo asymmetric divisions
- produce radial glial cell & a basal progenitor (= intermediate progenitor cell)

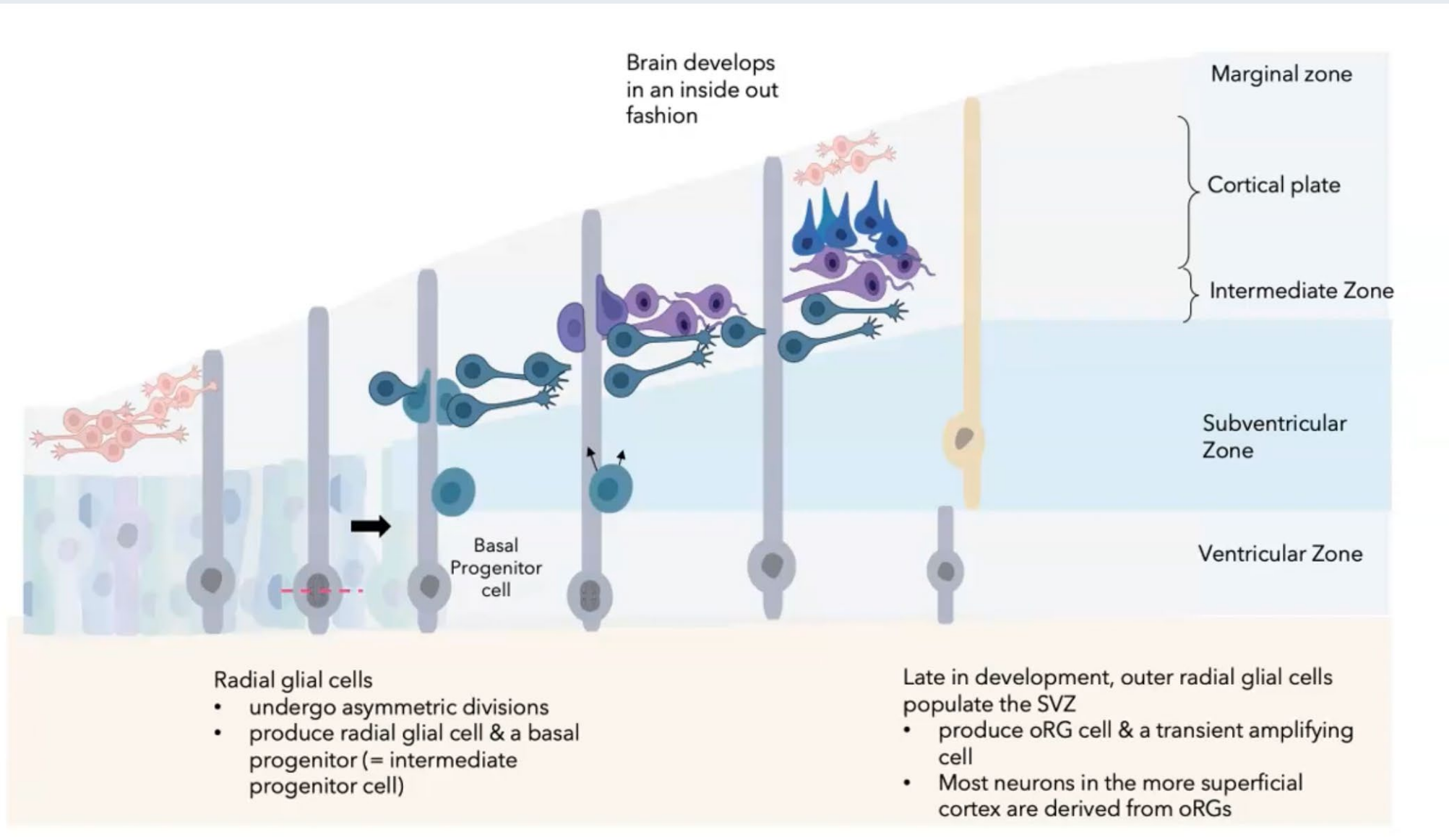
# Corticoneurogênese e Migração



# Corticoneurogênese e Migração

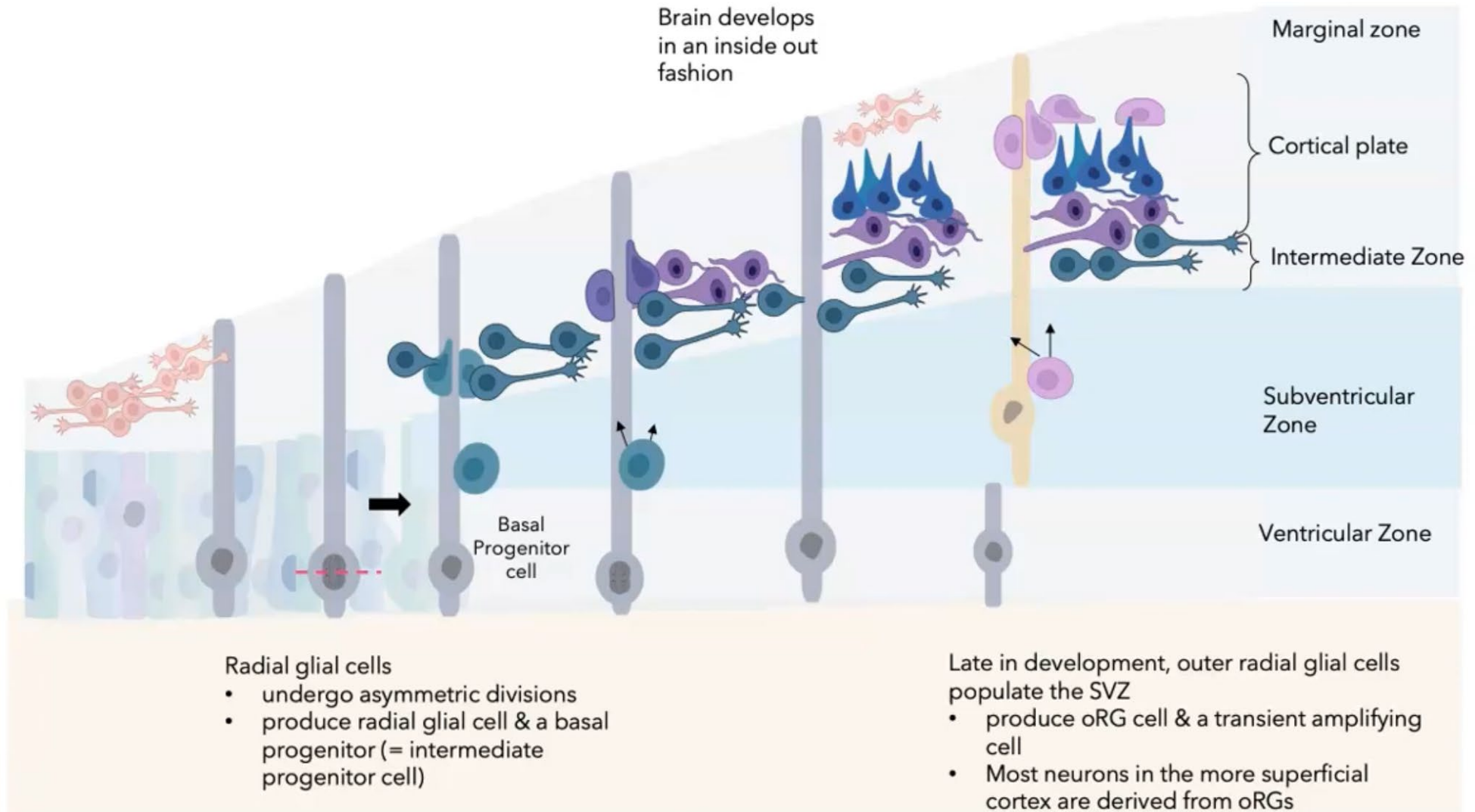


# Corticoneurogênese e Migração

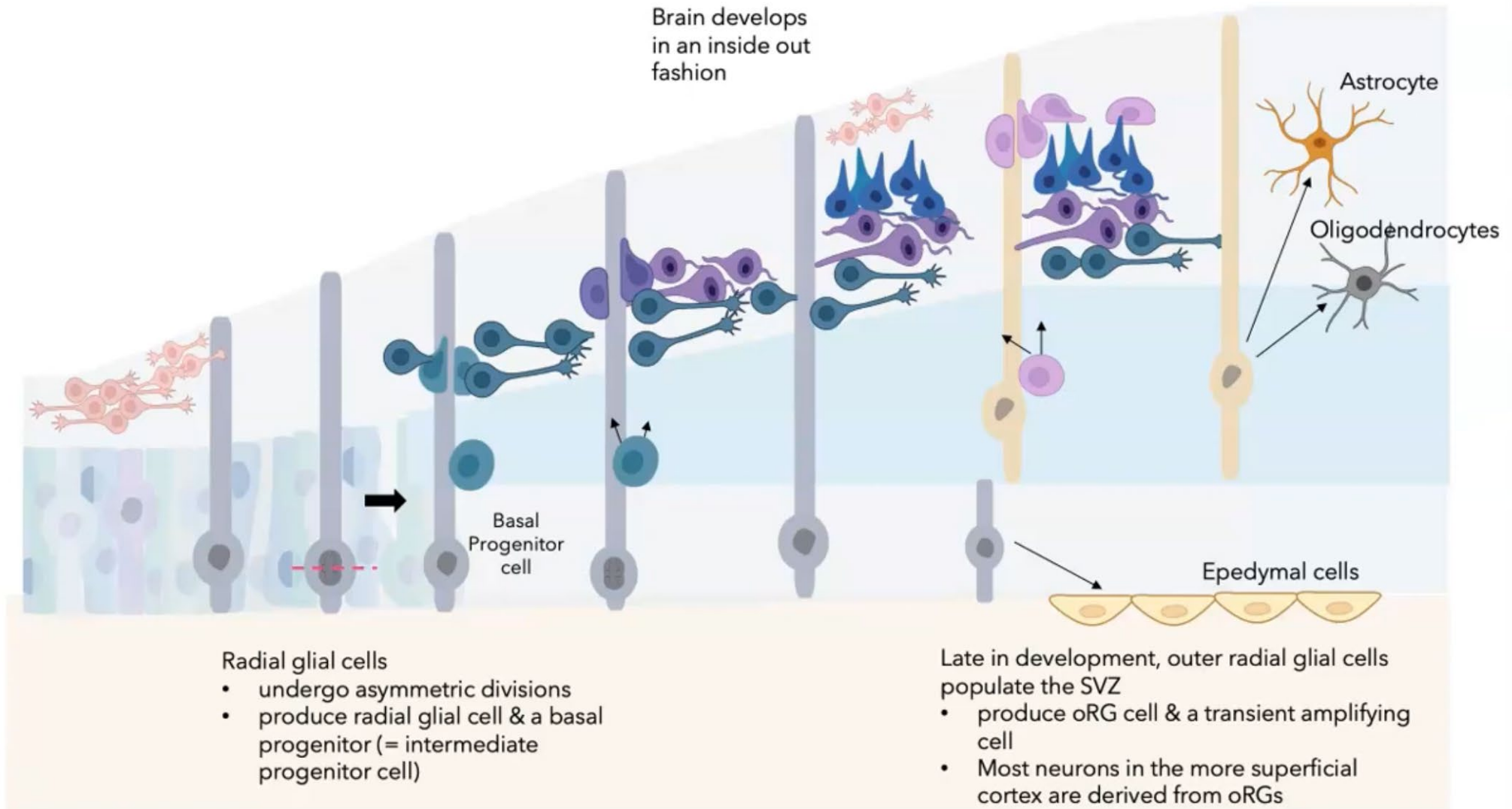




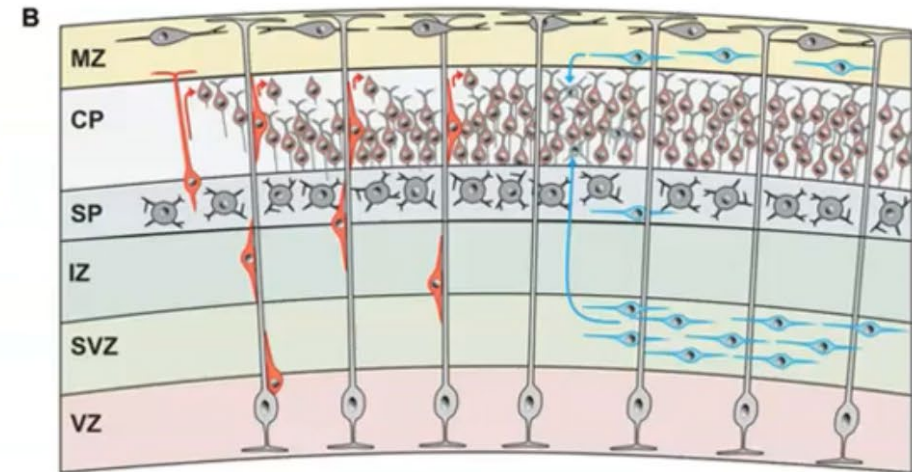
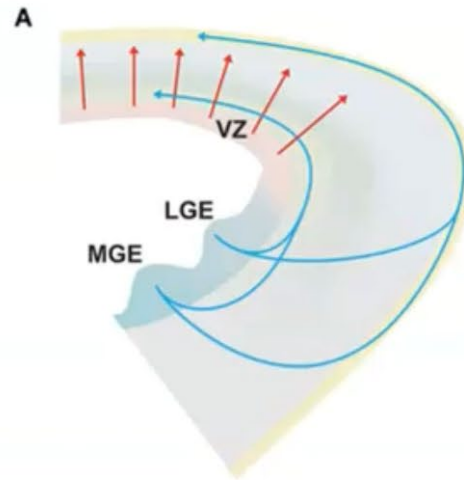
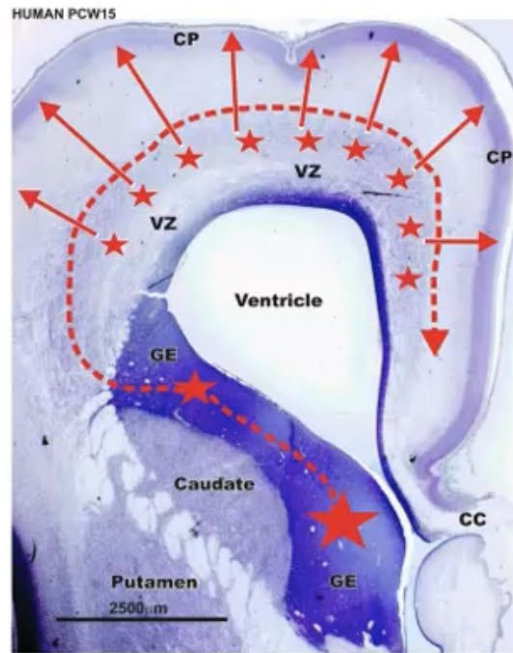
# Corticoneurogênese e Migração



# Corticoneurogênese e Migração

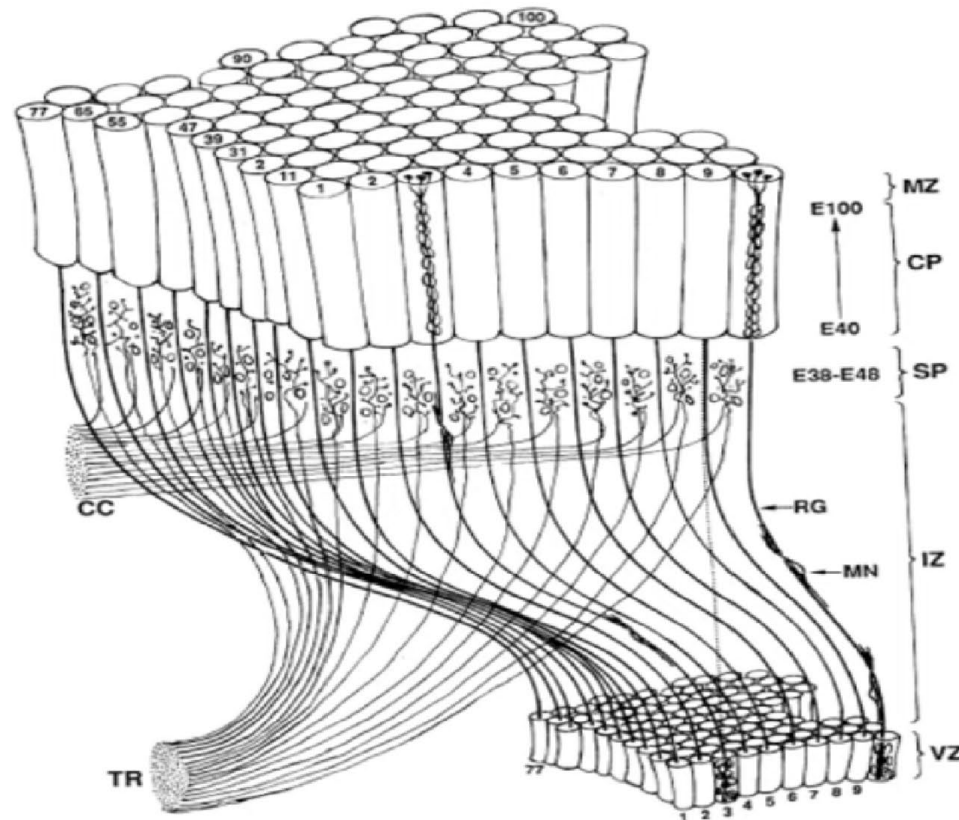


# Corticoneurogênese e Migração



# Corticoneurogênese e Migração

## The Radial Unit Hypothesis: A continuous radial glial scaffold

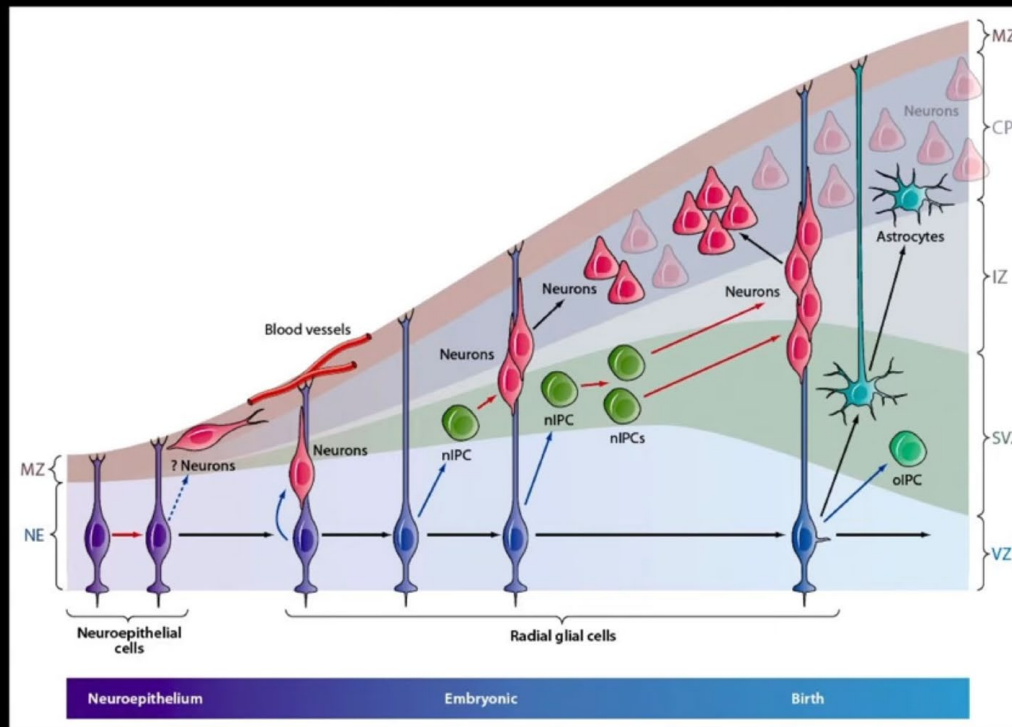


Rakic, P. (1988) Science

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# Corticoneurogênese e Migração

## The Mouse:



Kriegstein, A. & Alvarez-Buylla, A. (2009) Annu Rev Neurosci



iBiology.org

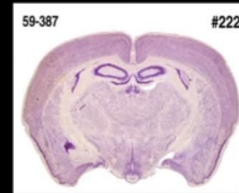
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# Corticoneurogênese e Migração

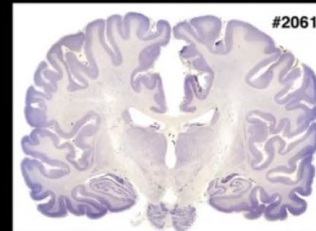
## Mouse vs Human Brain



mouse



human



*Comparative Mammalian Brain  
Collections*

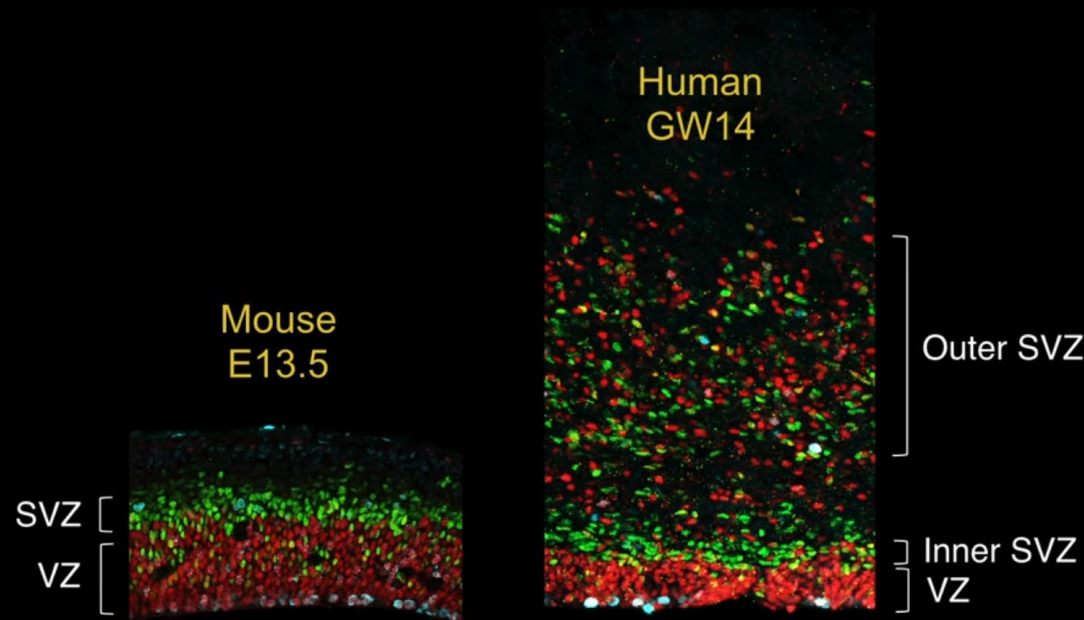
[www.brainmuseum.org](http://www.brainmuseum.org)

iBiology.org

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# Corticoneurogênese e Migração

What type of neural progenitor cells are found in the oSVZ?



Wang X., et al. (2011) Nat Neurosci

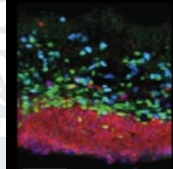
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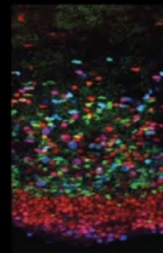
# Corticoneurogênese e Migração

The OSVZ expands during human cortex development

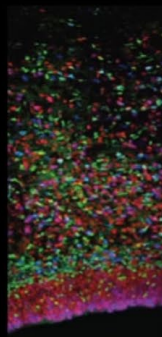
human



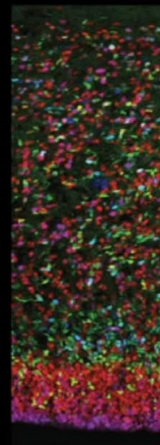
GW11.5



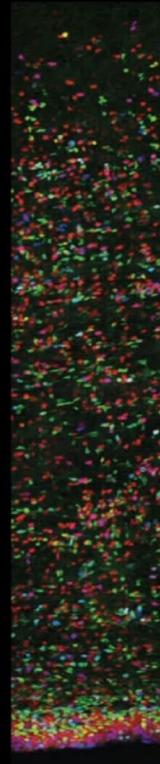
GW13



GW14



GW15.5



GW17

Hansen, DV, et al. (2010) Nature

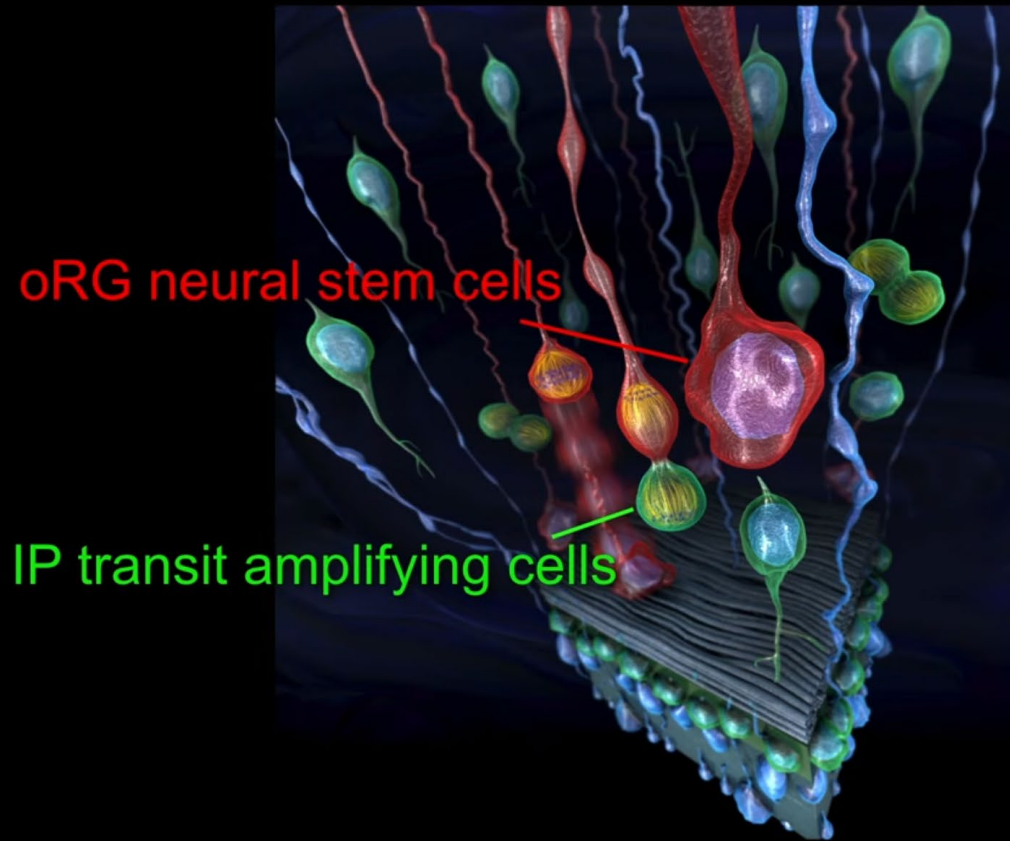


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# Corticoneurogênese e Migração

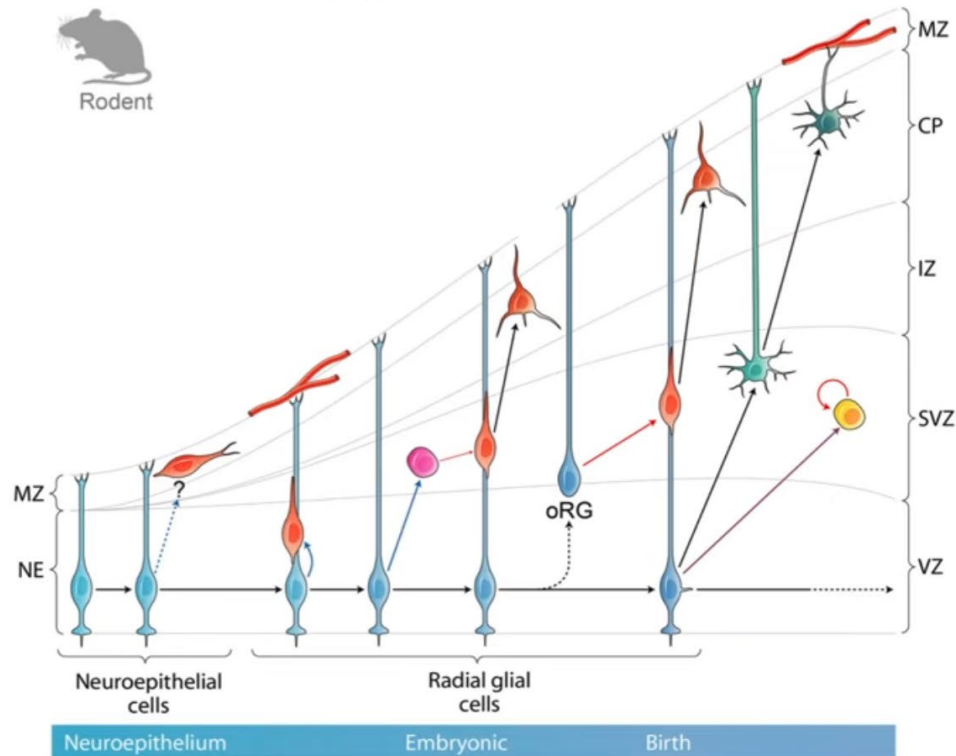


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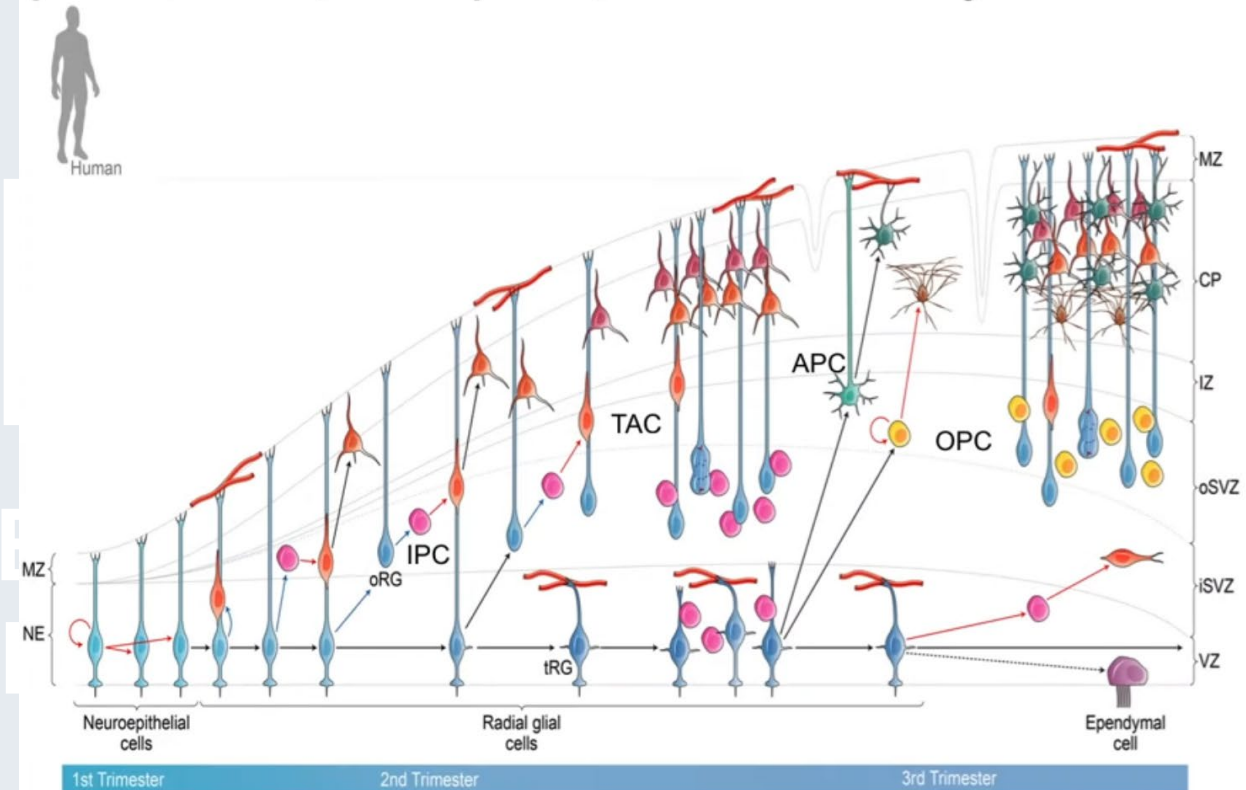
# Corticoneurogênese e Migração

Human cortical development: protracted, complex, and cellularly diverse



Neurodevelopmental Disorders & Function in the Healthy and Diseased Brain  
Chapter: Neural Stem Cells Among Glia By: Arturo Alvarez-Buylla & Arnold Kriegstein

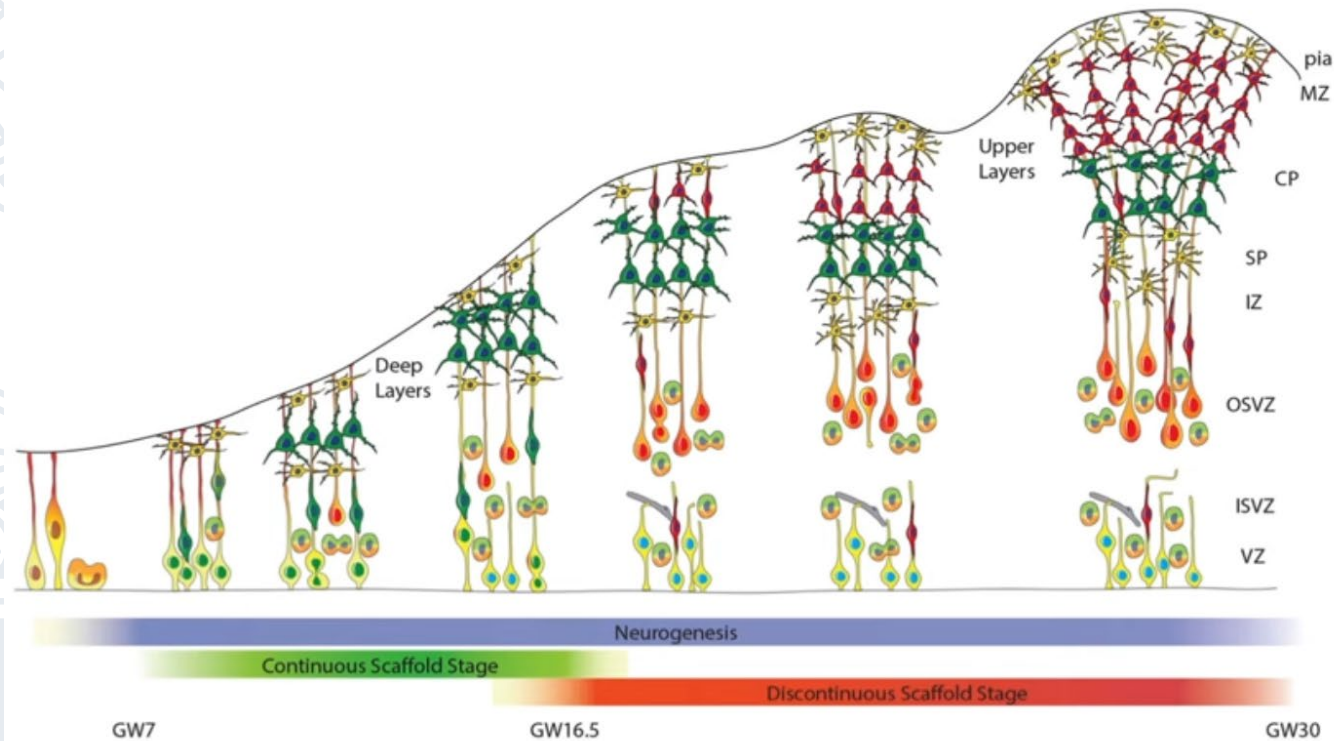
Human cortical development: protracted, complex, and cellularly diverse



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# Corticoneurogênese e Migração

## Supragranular Cortex Expansion Hypothesis

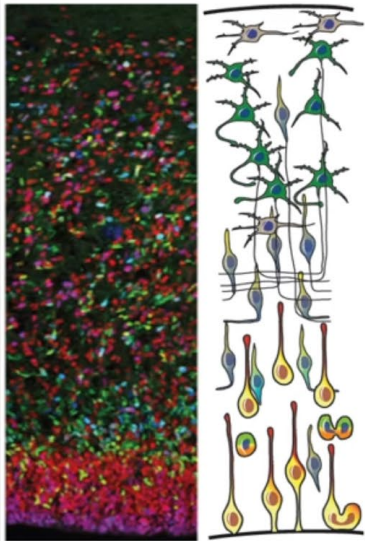


Nowakowski, TJ, et al. (2016) Neuron

DERAL  
O

# Corticoneurogênese e Migração

Single cell RNAseq to disentangle cellular composition



Pollen, AA, et al. (2015) Cell

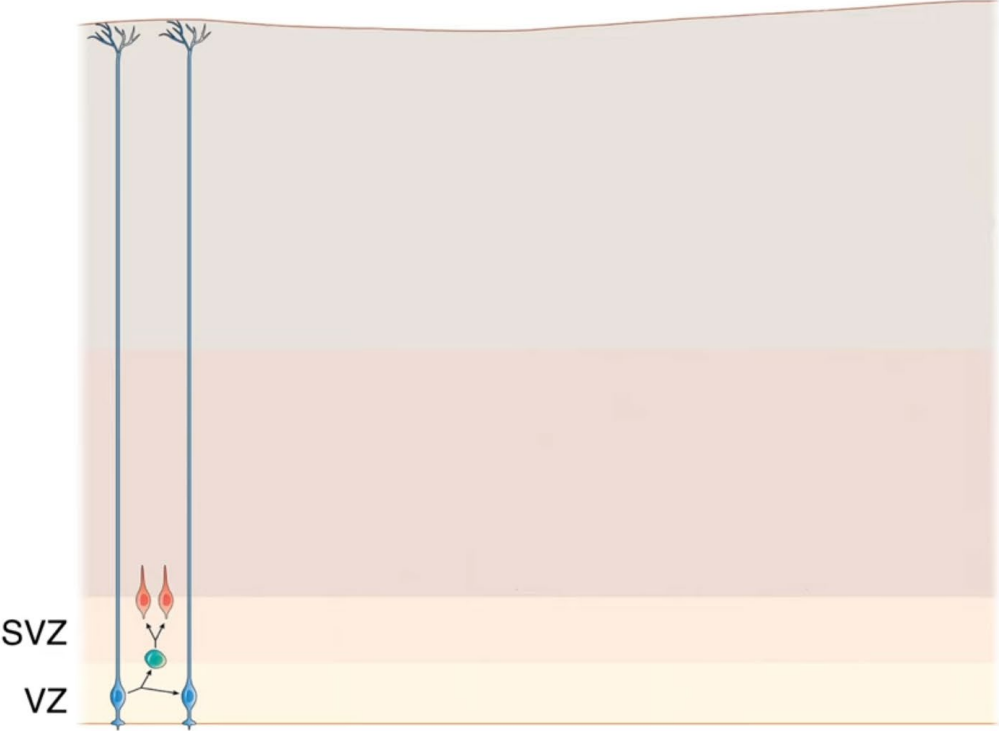


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# Corticoneurogênese e Migração

Schematic of human cortical development



The diagram illustrates the layers of the developing human cortex. It shows a vertical cross-section with a light brown upper layer and a yellow lower layer. Two vertical lines represent the migration of neurons from the ventricular zone (VZ) at the bottom to the subventricular zone (SVZ) and then to the cortical plate. The VZ is labeled at the bottom left, and the SVZ is labeled above it. The diagram shows the migration of neurons from the VZ to the SVZ and then to the cortical plate. The SVZ is shown as a layer of cells that is formed during development. The VZ is shown as a layer of cells that is formed during development. The diagram shows the migration of neurons from the VZ to the SVZ and then to the cortical plate. The SVZ is shown as a layer of cells that is formed during development. The VZ is shown as a layer of cells that is formed during development.

SVZ

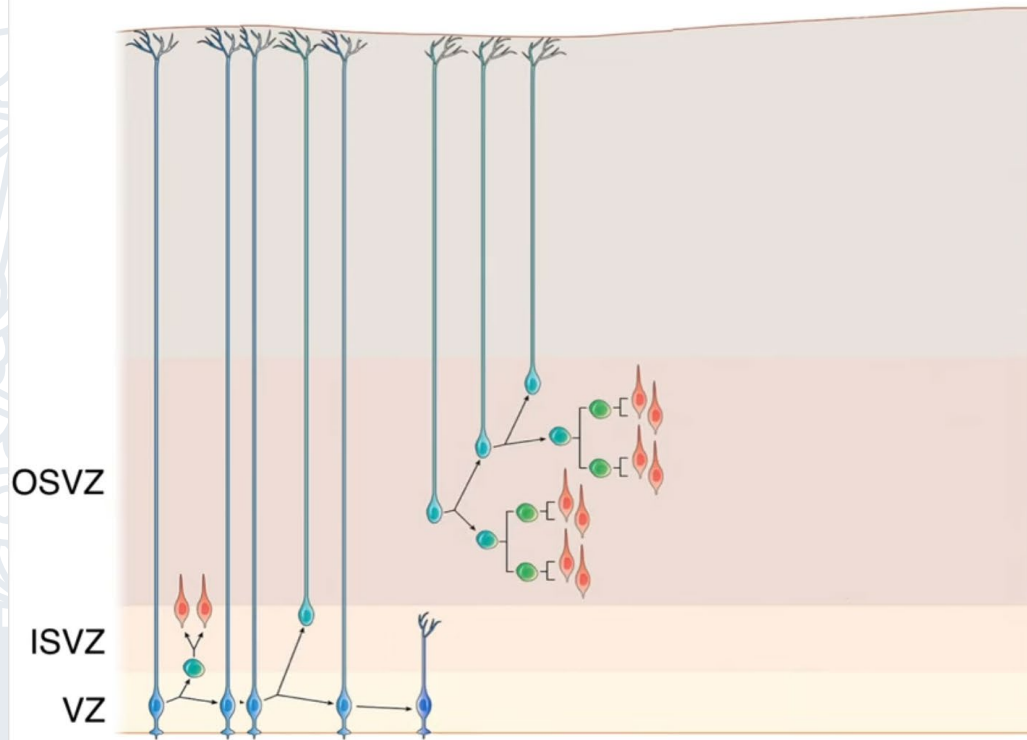
VZ

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# Corticoneurogênese e Migração

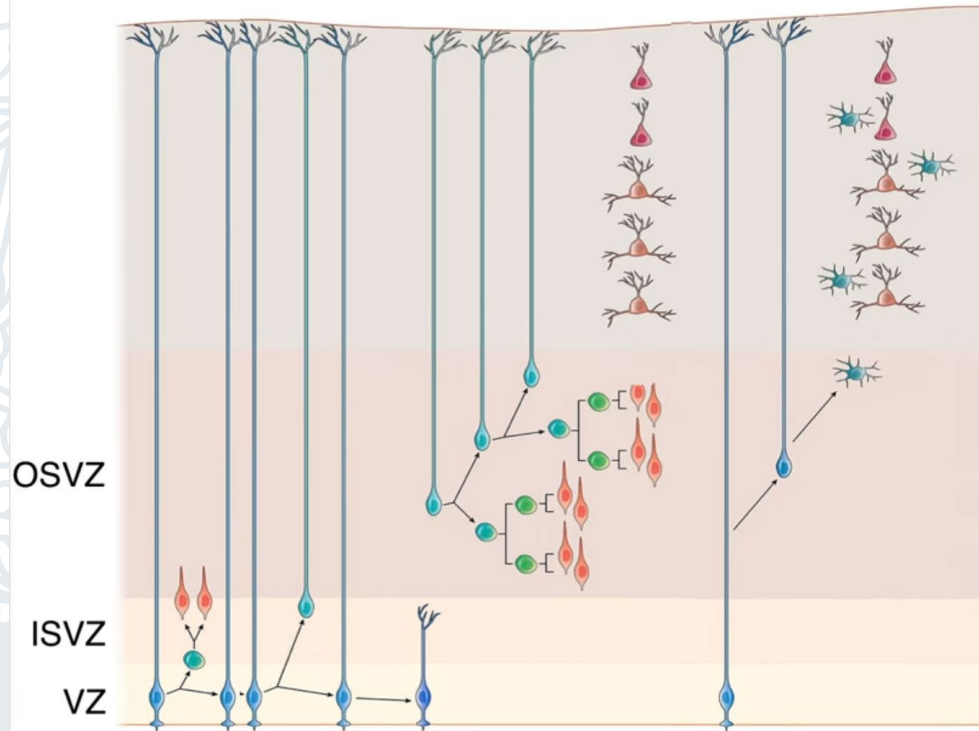
Schematic of human cortical development



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# Corticoneurogênese e Migração

Schematic of human cortical development



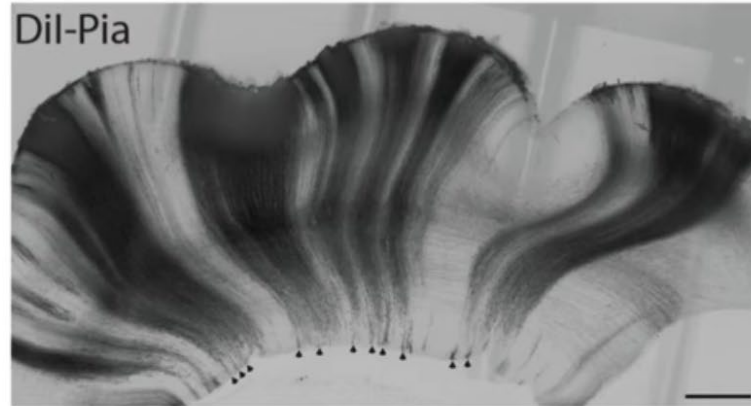
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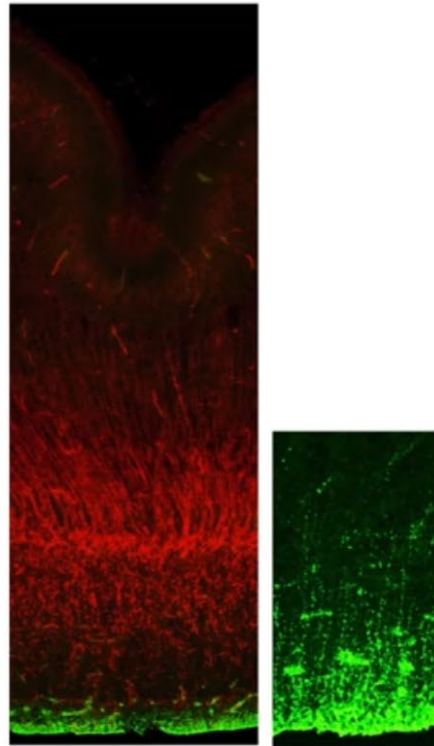
# Corticoneurogênese e Migração

A discontinuous glial scaffold in humans

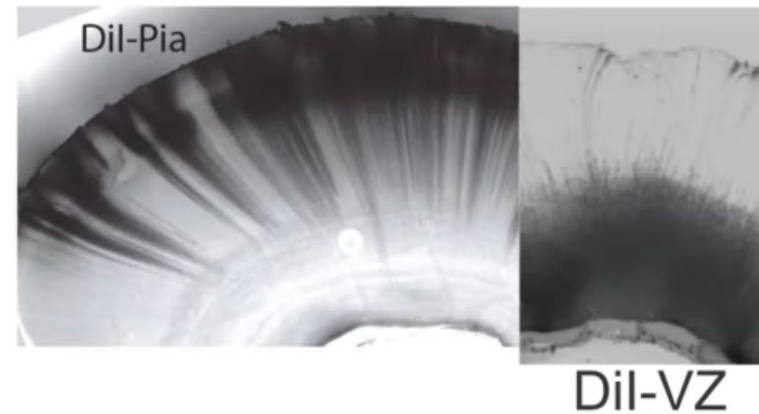
GW15



GW18



GW18



Nowakowski, TJ, et al. (2016) Neuron

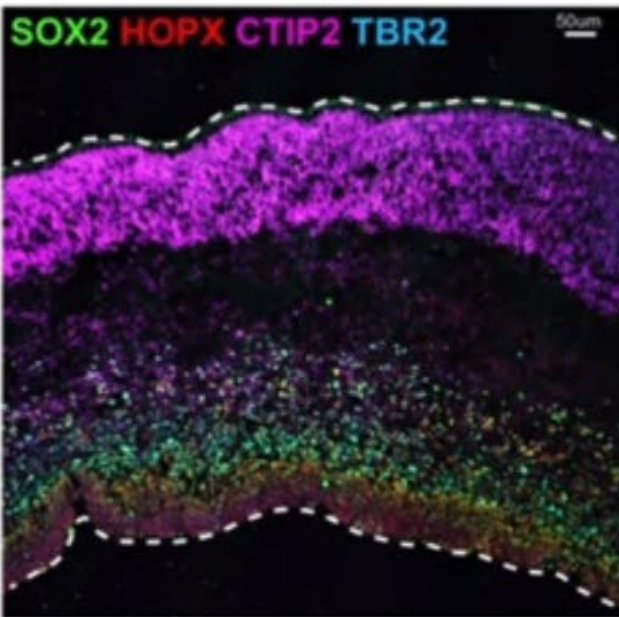
DERAL  
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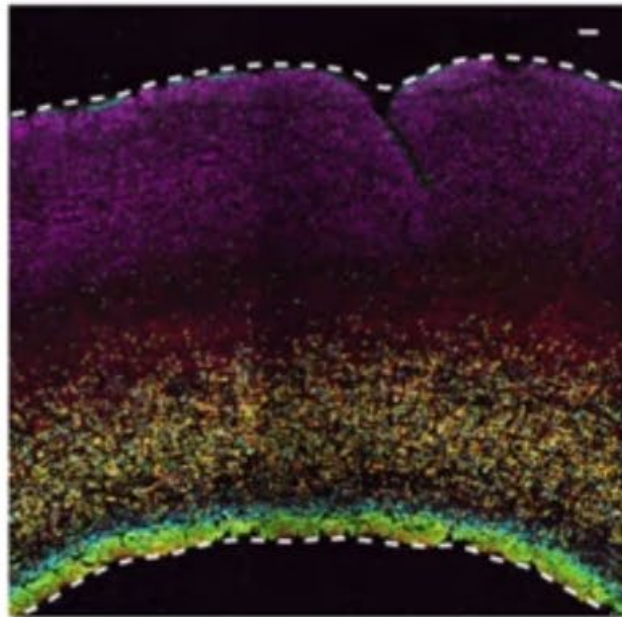
# Corticoneurogênese e Migração

*Fetal tissue*

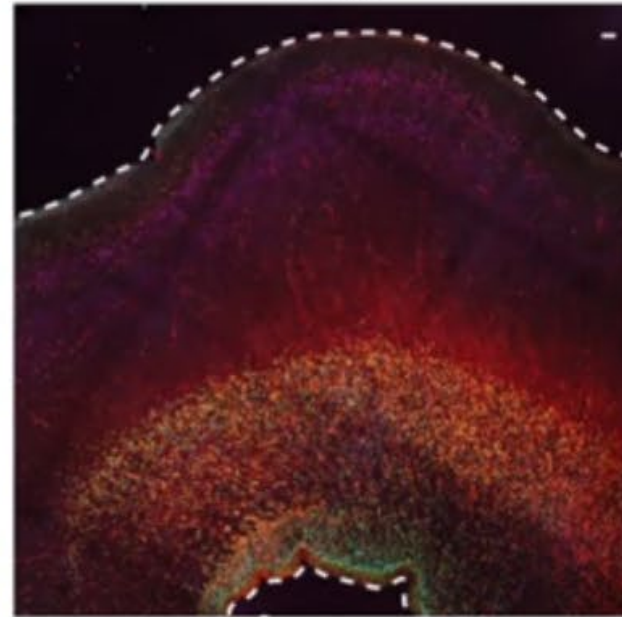
GW13



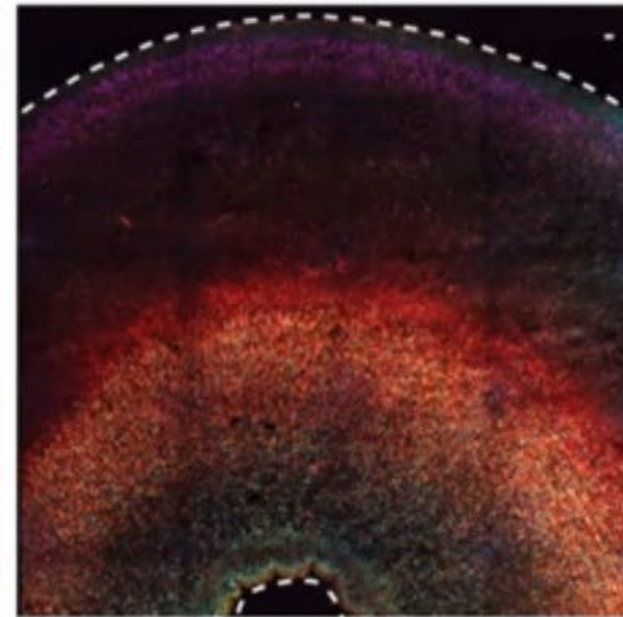
GW15



GW17



GW19



# Conclusões de Kriegstein

- No desenvolvimento do córtex humano verifica-se uma diversidade de células precursoras não encontrada em roedores.
- A glia radial externa é particularmente abundante durante o desenvolvimento do córtex humano.
- A glia radial externa contribui para o crescimento e a expansão cortical, particularmente nas camadas corticais superiores.

# Considerações Finais

Quando cessa a corticoneurogênese



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# AULAS Arnold Kriegstein (UCSF)

(1) Outer Subventricular Zone Radial Glia Cells - Brain

Development:

[https://www.youtube.com/watch?v=9mCBjA8wxrI&list=PLYzr2iF\\_d\\_i53cYdWxd5WRXZihz7KpjR0h&index=2](https://www.youtube.com/watch?v=9mCBjA8wxrI&list=PLYzr2iF_d_i53cYdWxd5WRXZihz7KpjR0h&index=2)

(2) Cerebral Organoids: Models of Human Brain Disease and Evolution:

<https://www.youtube.com/watch?v=G5IAKRkUH40>