Neuro-Immnue regulation of Brain Development

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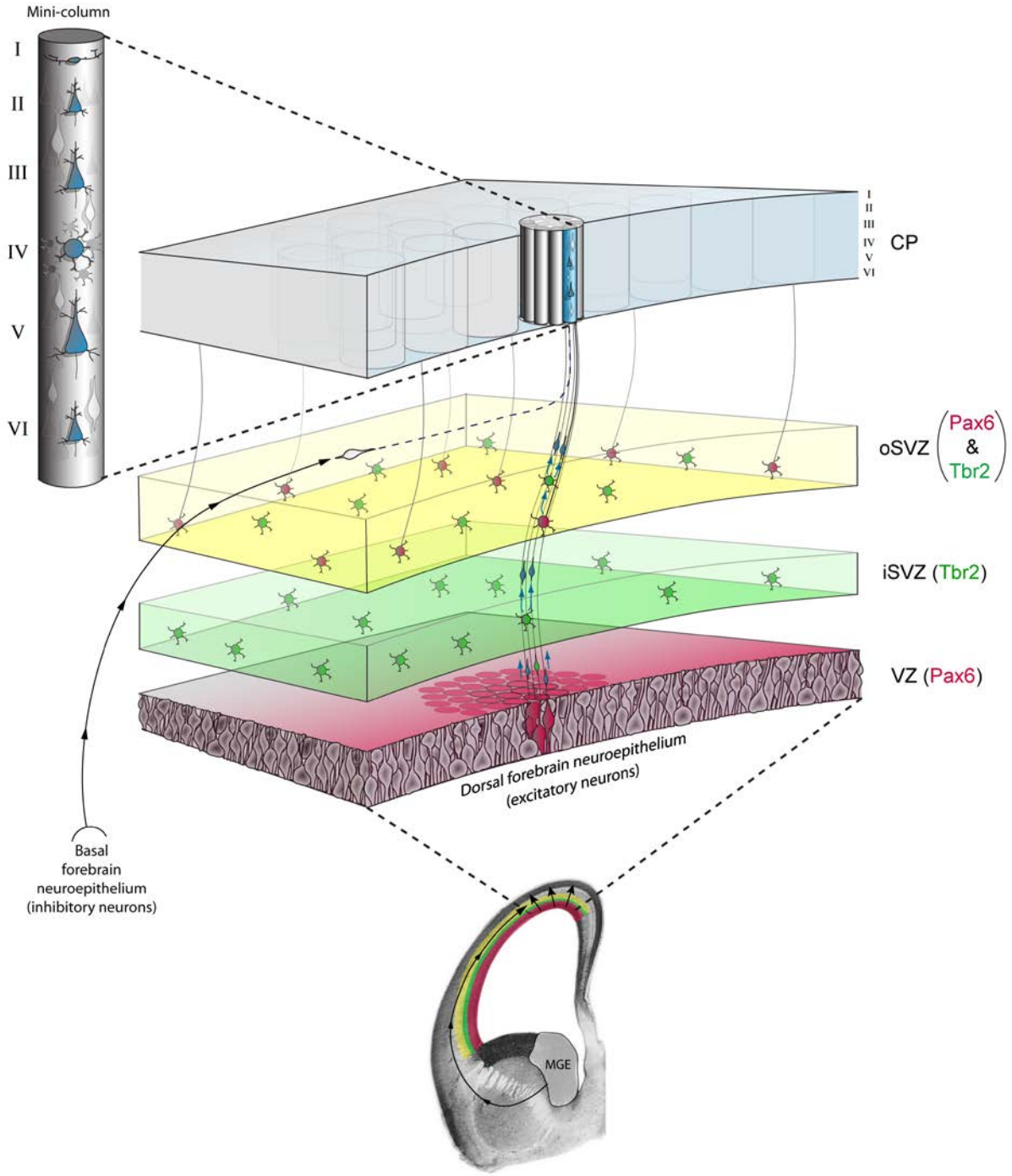
Human

GW11

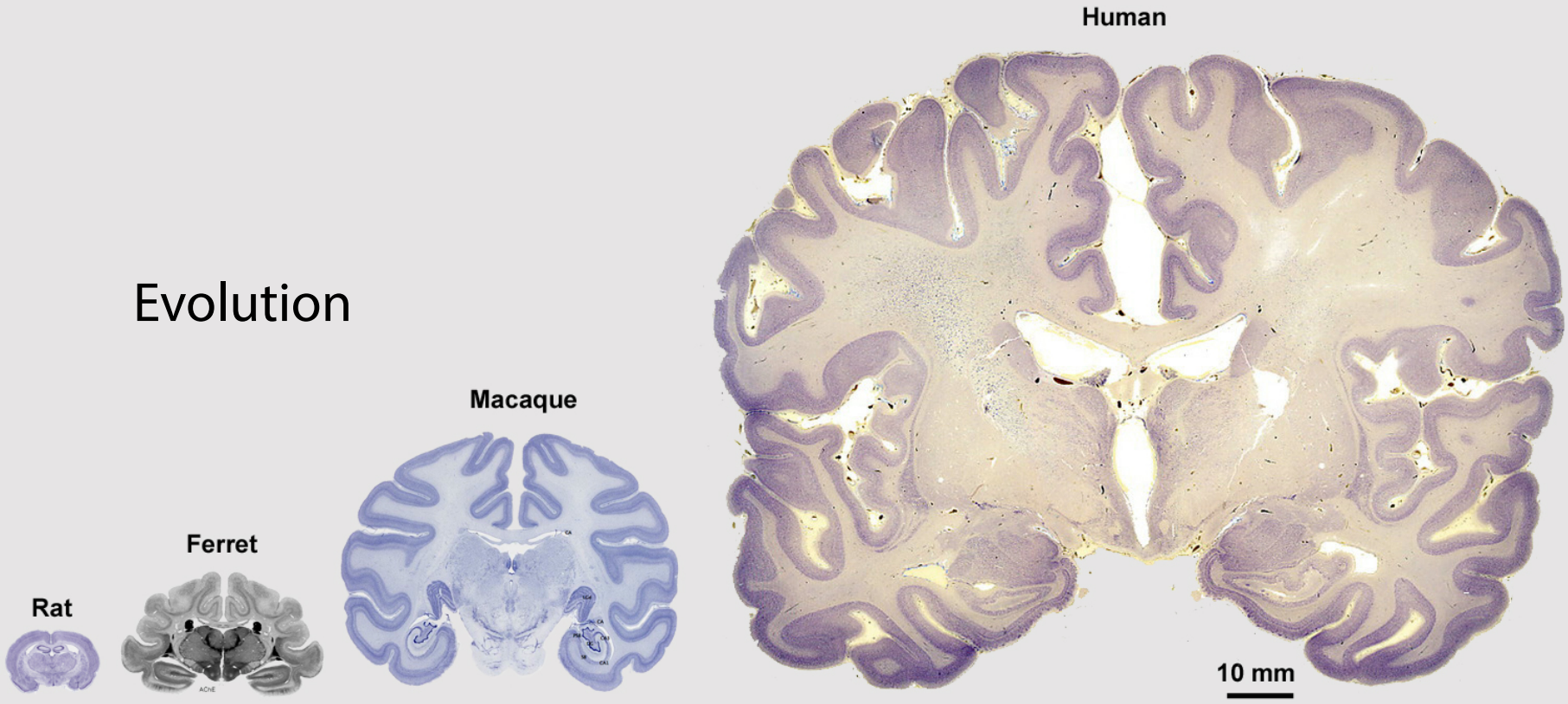
GW3

10 mm

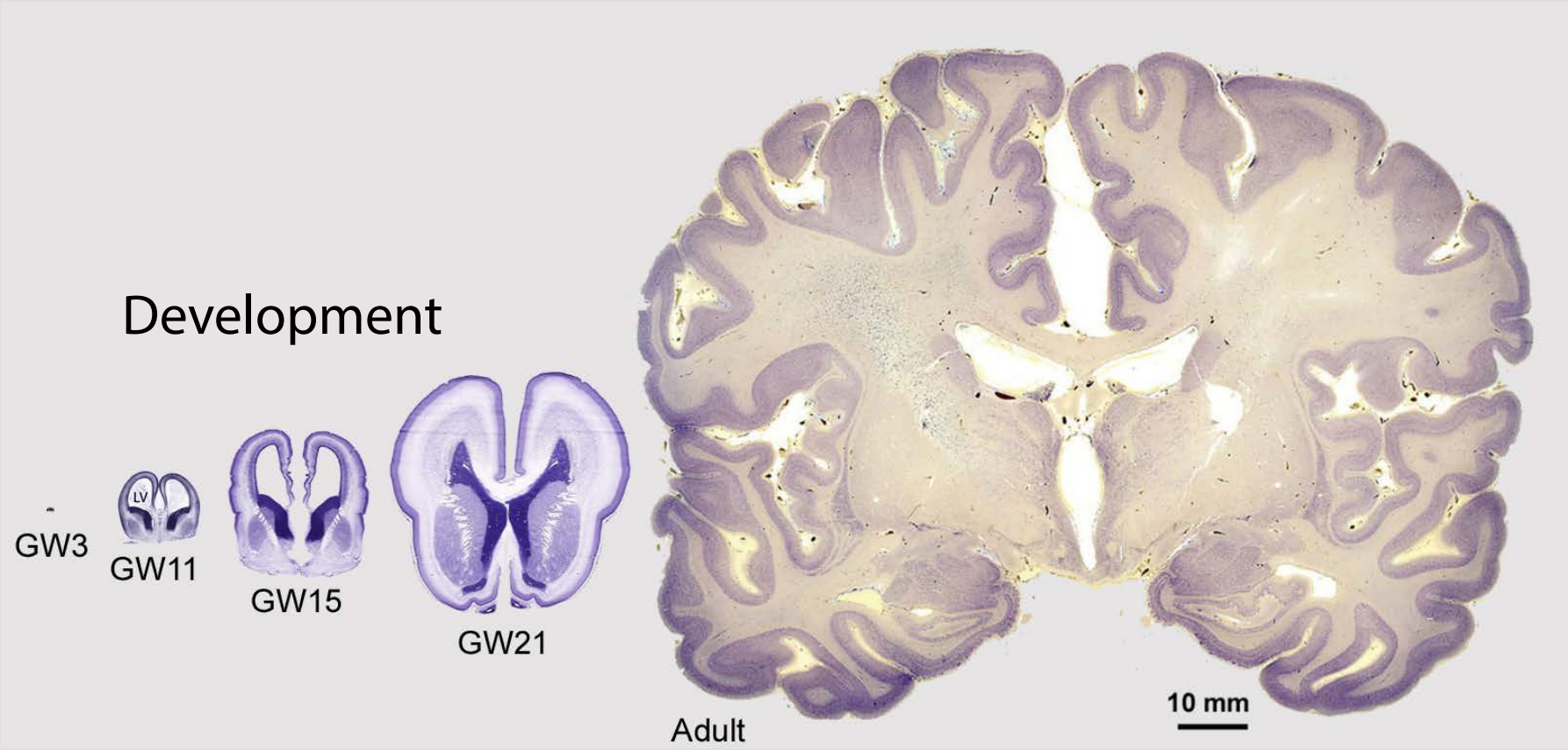

Mini-column
I
II
III
IV
V
VI
CP
oSVZ
Pax6
&
Tbr2
iSVZ (Tbr2)
VZ (Pax6)
Dorsal forebrain neuroepithelium
(excitatory neurons)
Basal
forebrain
neuroepithelium
(inhibitory neurons)
MGE

How is cortical expansion achieved?

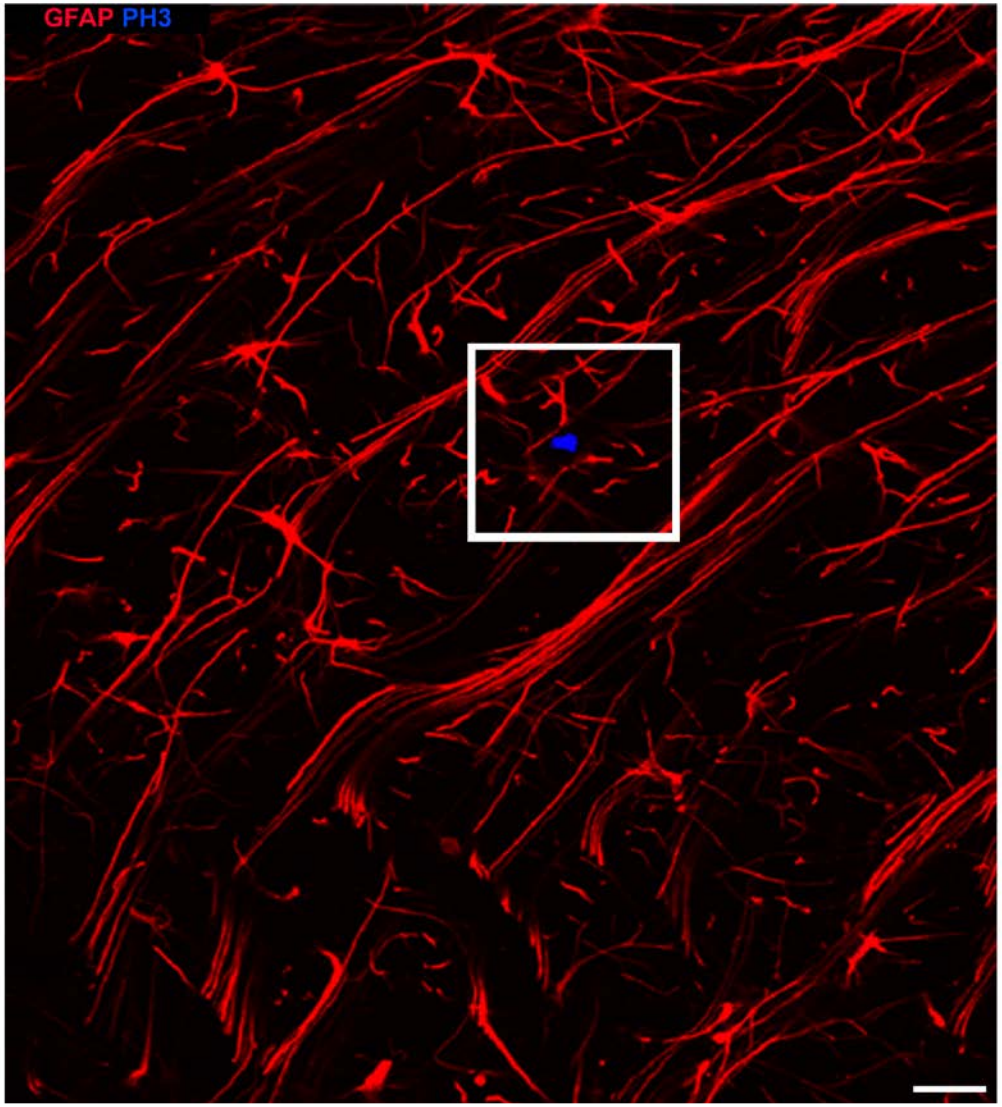
Evolution

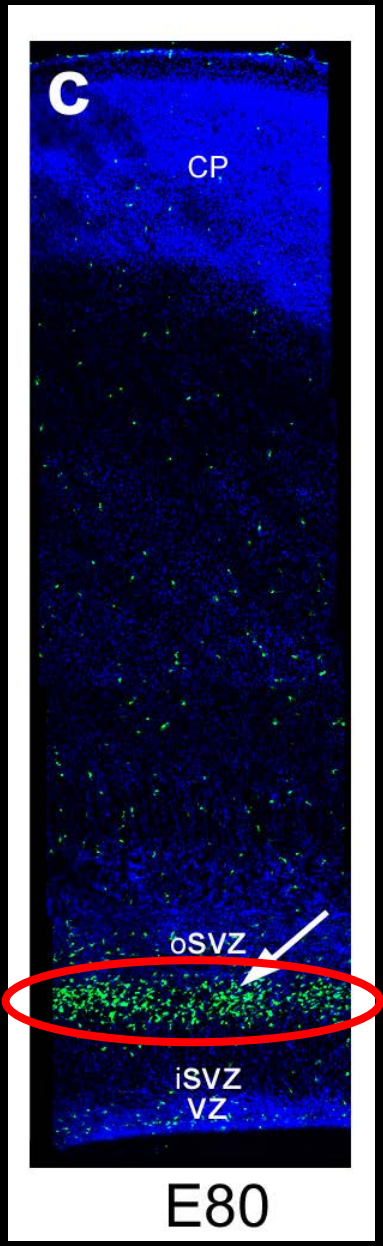


How is cortical expansion achieved?



1) Mechanisms promoting growth ⟷ 2) Mechanisms restraining growth


GFAP PH3


C
CP
oSVZ
iSVZ
VZ
E80

What are microglia?

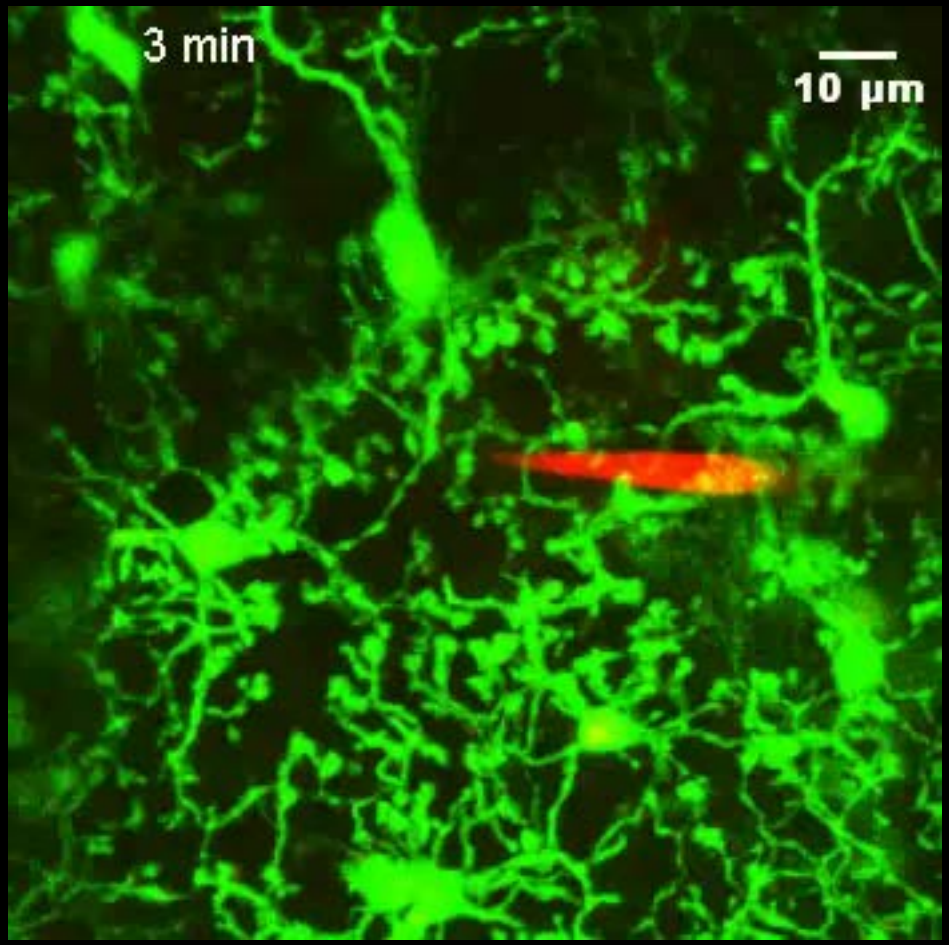
Del Rio-Hortega, 1919

Initial Descriptions: (Pio del Rio-Hortega)

1) enter the brain during early development
2) can have amoeboid morphology, of mesodermal origin
3) use vessels and white matter tracts as guides for migration
4) enter all brain regions
4) branched, ramified morphological phenotype in the mature brain
5) in mature brain are evenly dispersed
6) each cell occupies a defined territory.
7) after pathological event undergo a transformation
8) transformed cells have amoeboid morphology similar to development
9) capacity to migrate, proliferate and phagocytose

Rapidly respond to stimuli / foreign pathogens

Rapidly respond to stimuli / foreign pathogens



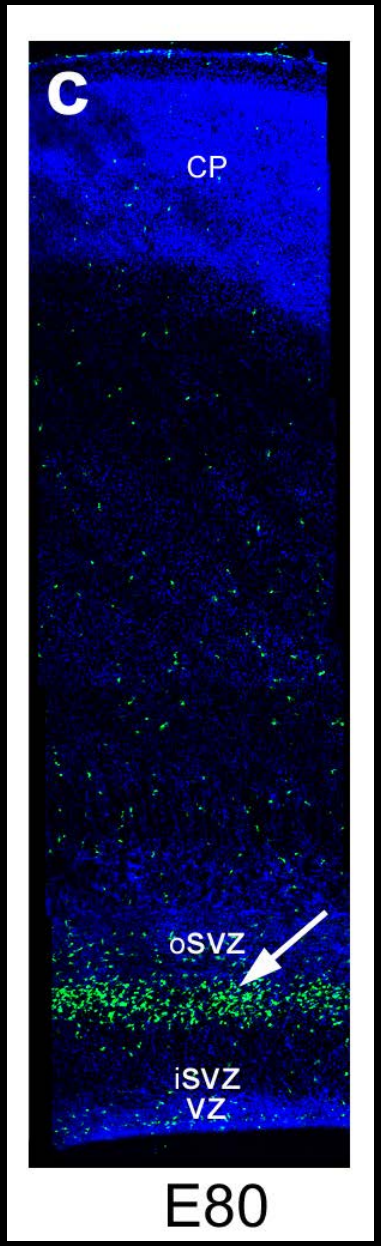
Davalos et al., 2005 Nat Neurosci

5% of all cells in the adult brain

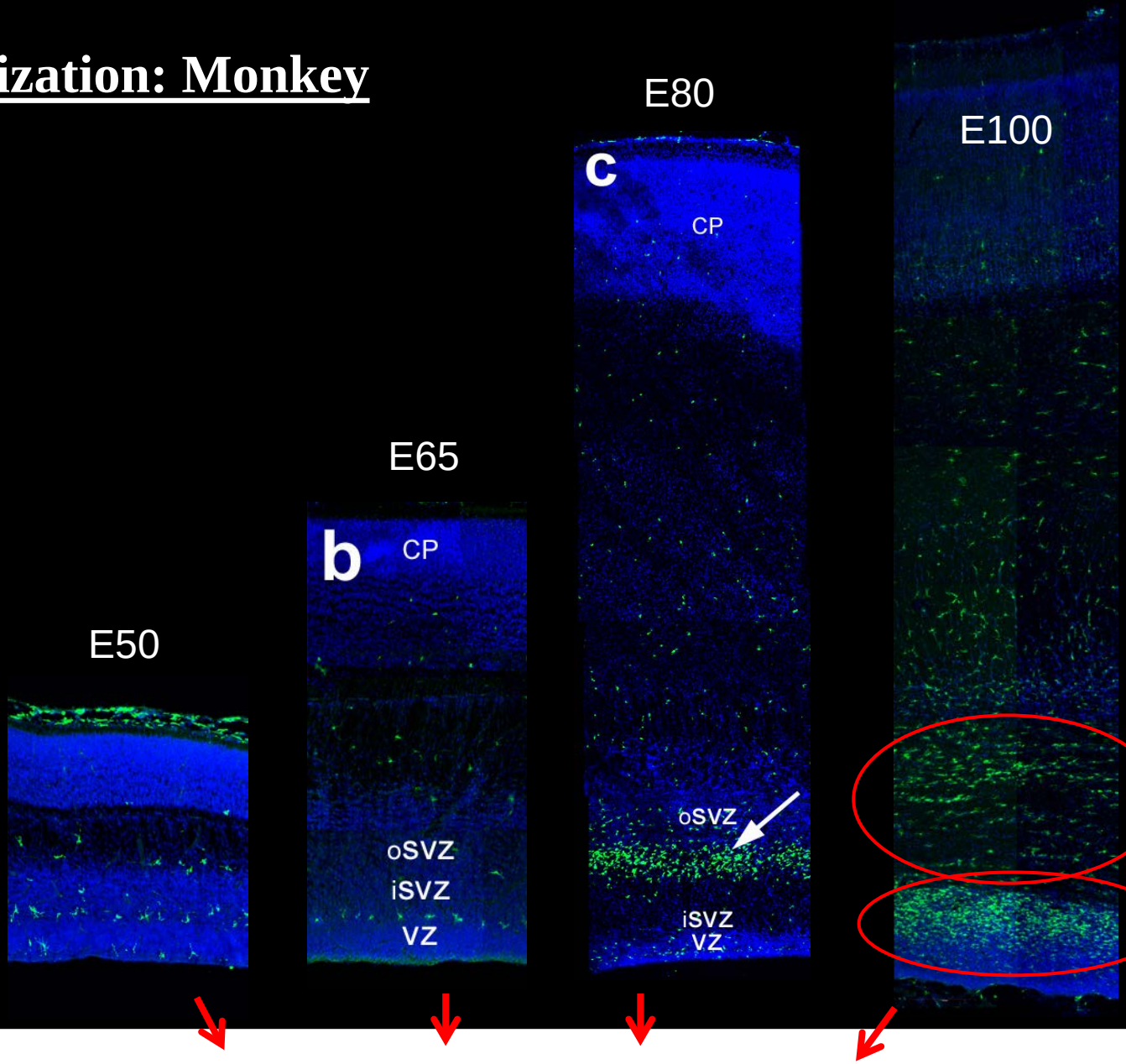
Very little known about microglial function in the prenatal brain

1. Mechanisms that promote growth:

2. Mechanisms that restrain growth: **Microglia?**



I. Colonization: Monkey

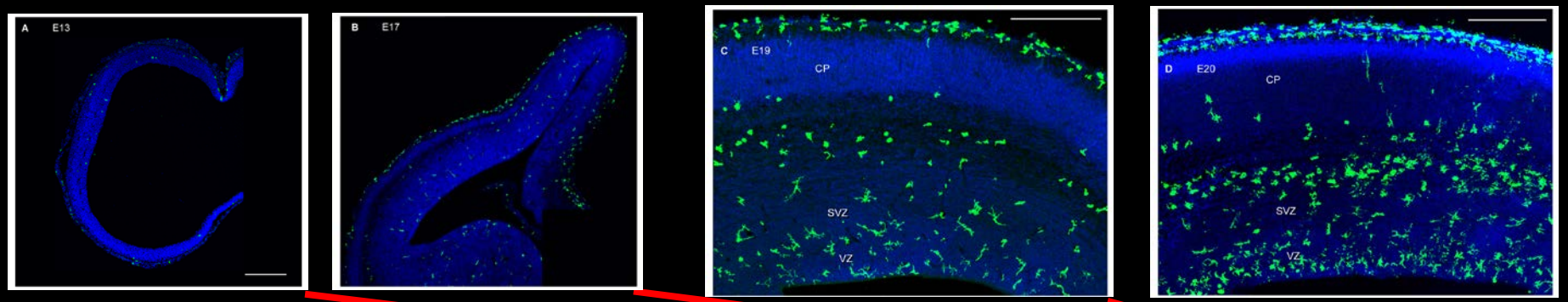


Macaque **GD165**

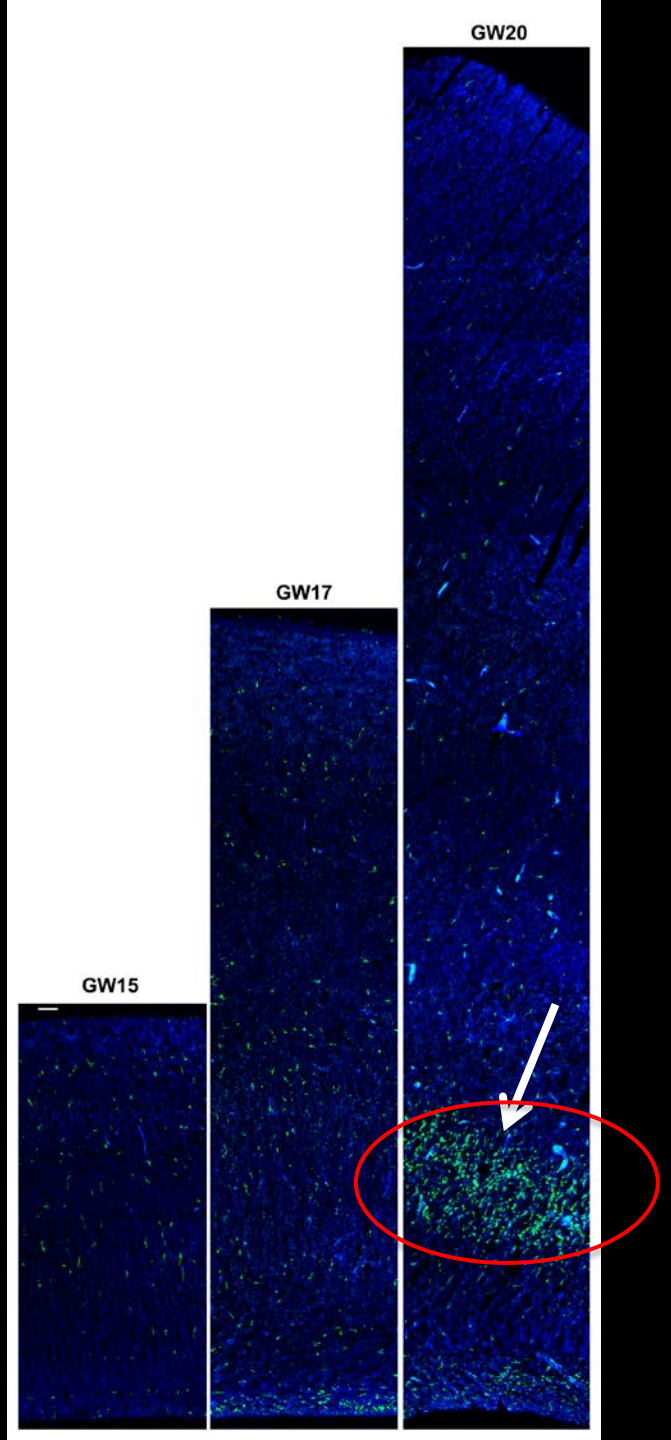
1st trimester | 2nd trimester, *Neurogenesis* | 3rd trimester

I. Colonization: Rat

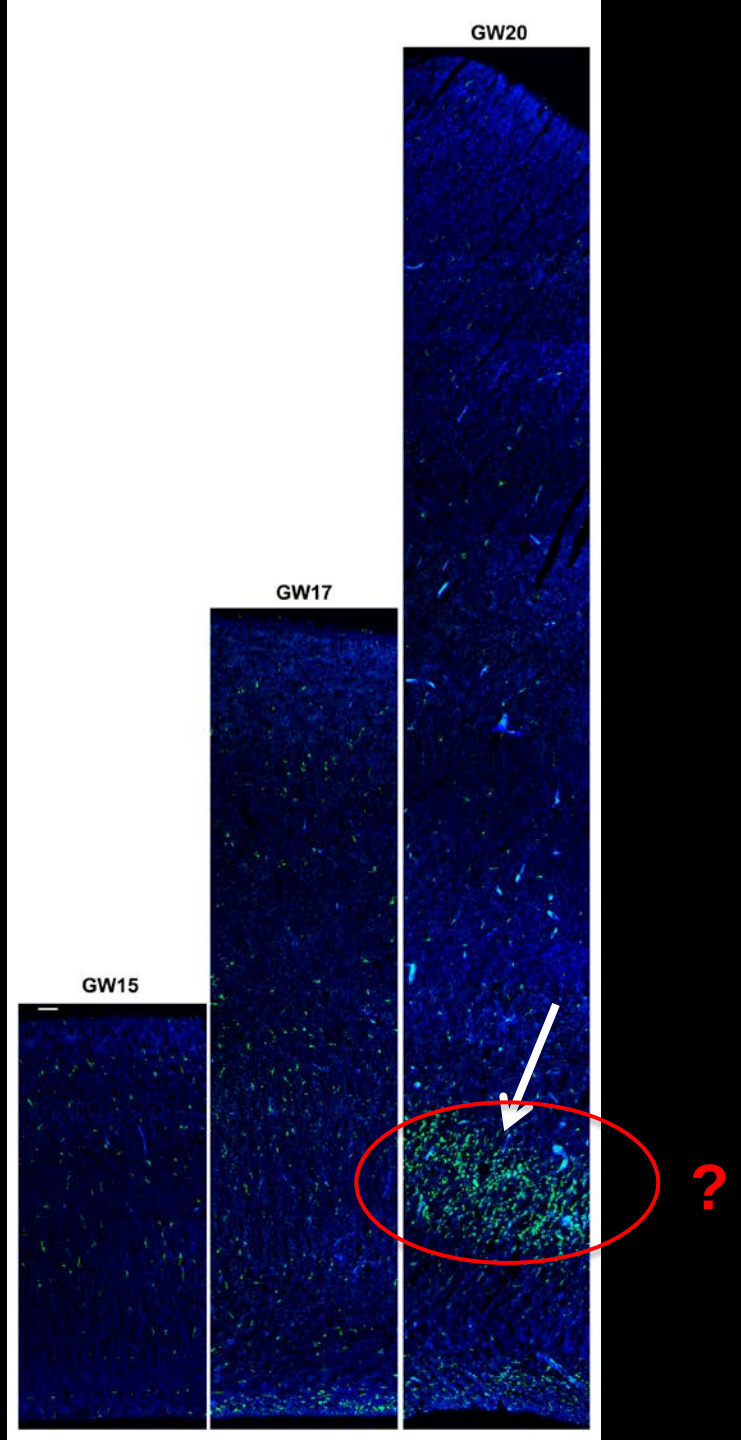
- Microglia enter rat cortex ~E12
- Remain sparse through E17
- Begin colonizing proliferative zones heavily ~E19
- Fill proliferative zones by E20



Same general pattern
in fetal human cortex

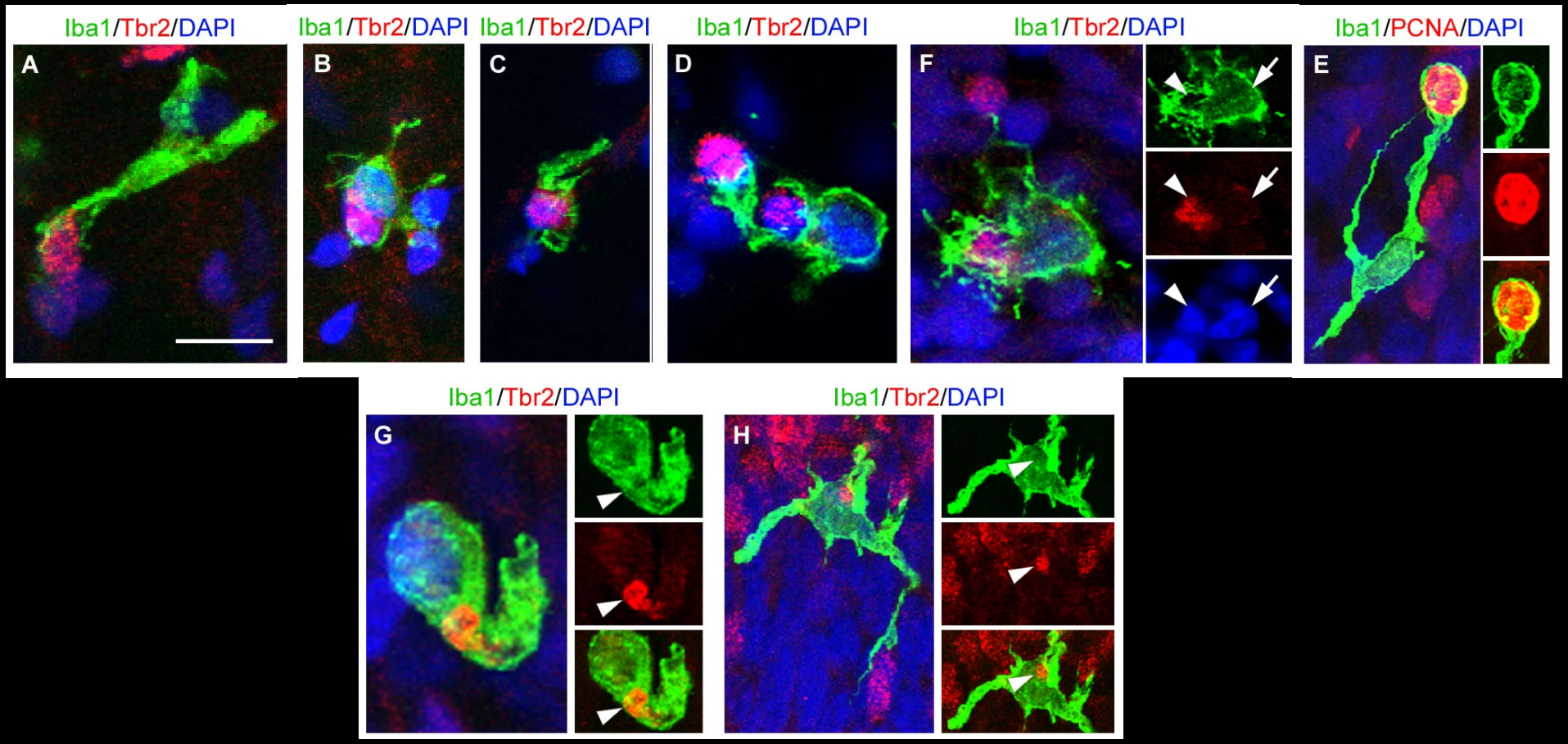


1. Microglia
2. Primary NPCs
3. Secondary NPCs



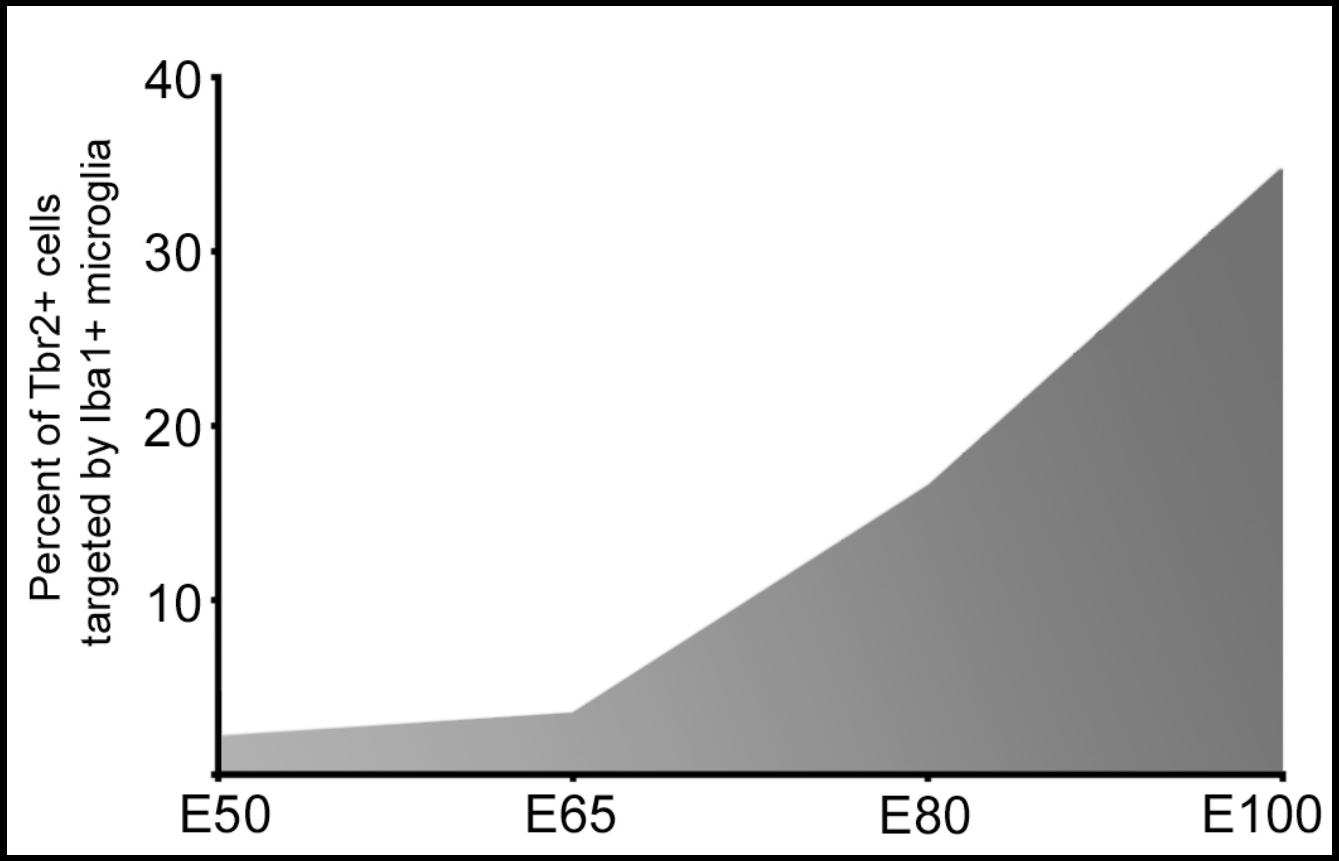
II. Function

Microglia phagocytose neural precursor cells in the fetal brain

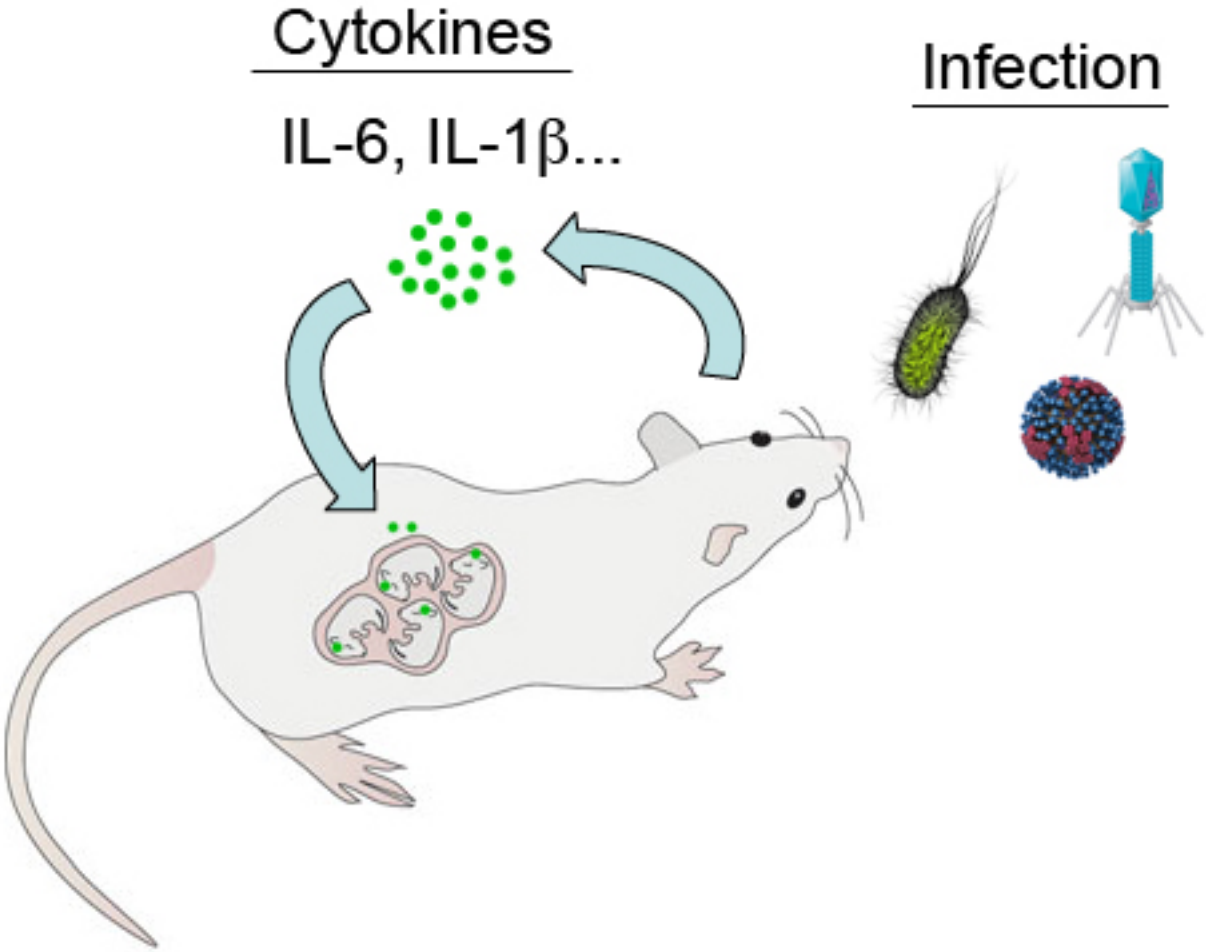


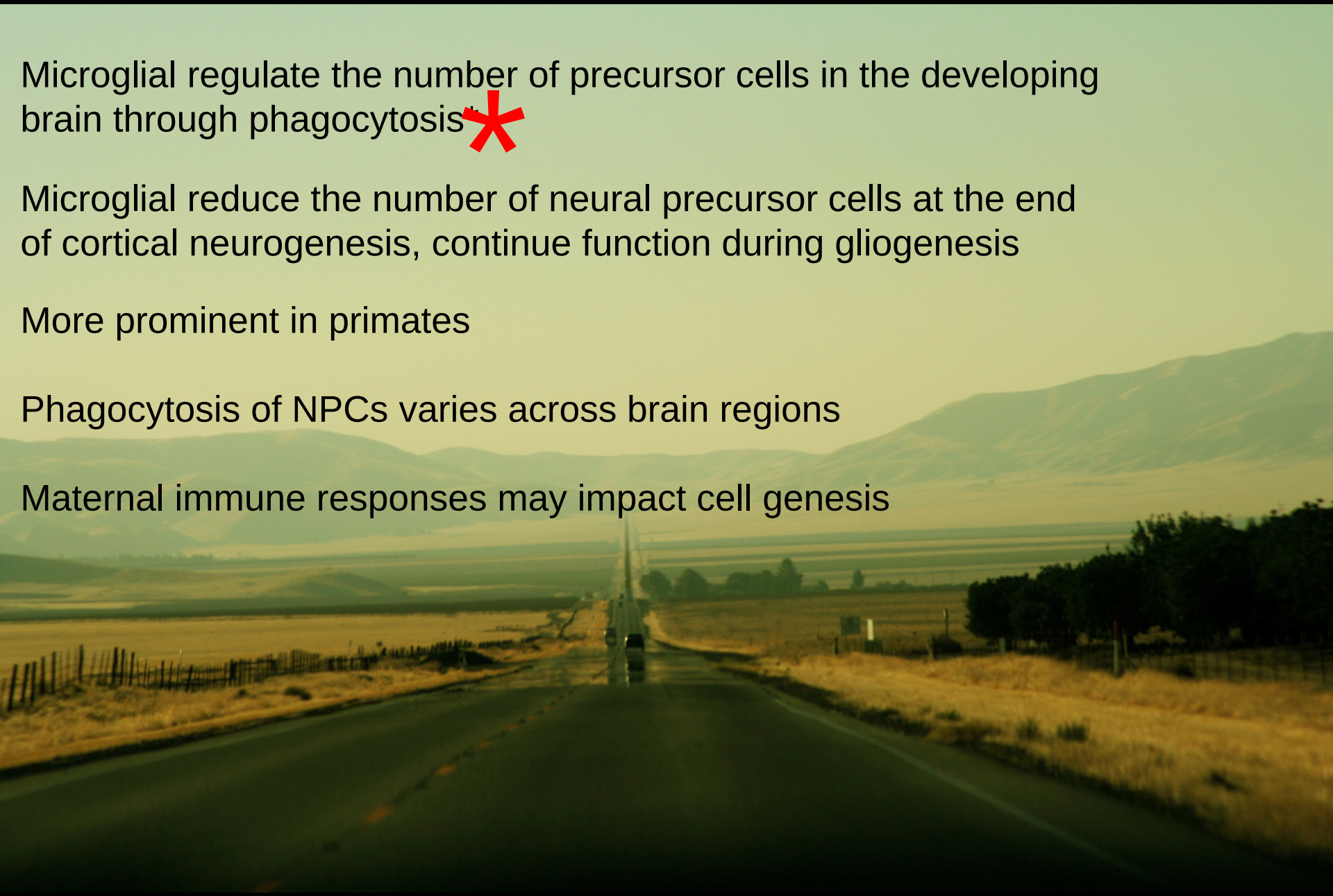
II. Function

Proportion of targeted NPCs, in cortex, ↑ during development



Maternal Immune Activation





Microglial regulate the number of precursor cells in the developing brain through phagocytosis*

Microglial reduce the number of neural precursor cells at the end of cortical neurogenesis, continue function during gliogenesis

More prominent in primates

Phagocytosis of NPCs varies across brain regions

Maternal immune responses may impact cell genesis

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