



International Staff Training Week
Disabilities and Integration

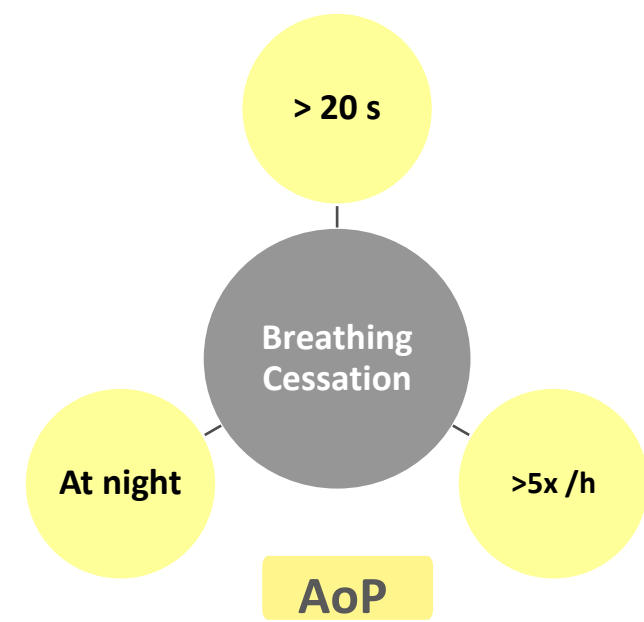
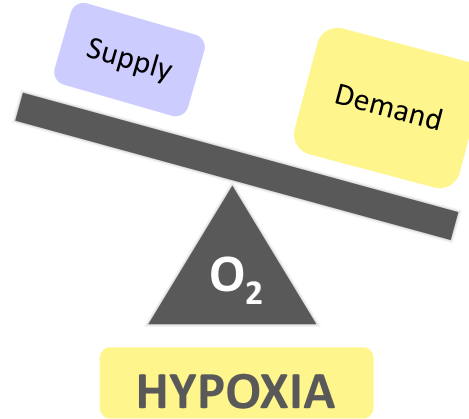
**Cellular and molecular
alterations induced by Apnea
of Prematurity in the murine
cerebellum.**

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Thesis Advisor: Dr Delphine Burel

Apnea of Prematurity (AoP)

Definition

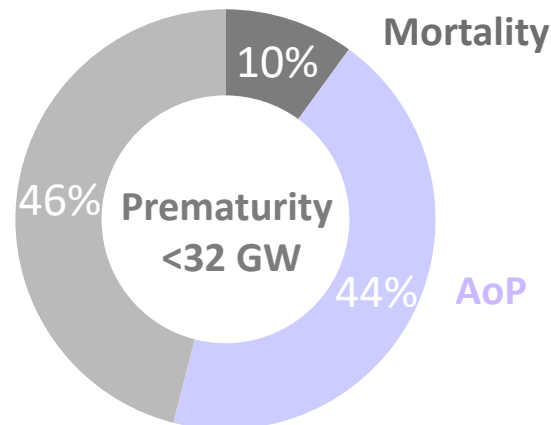


Consequences



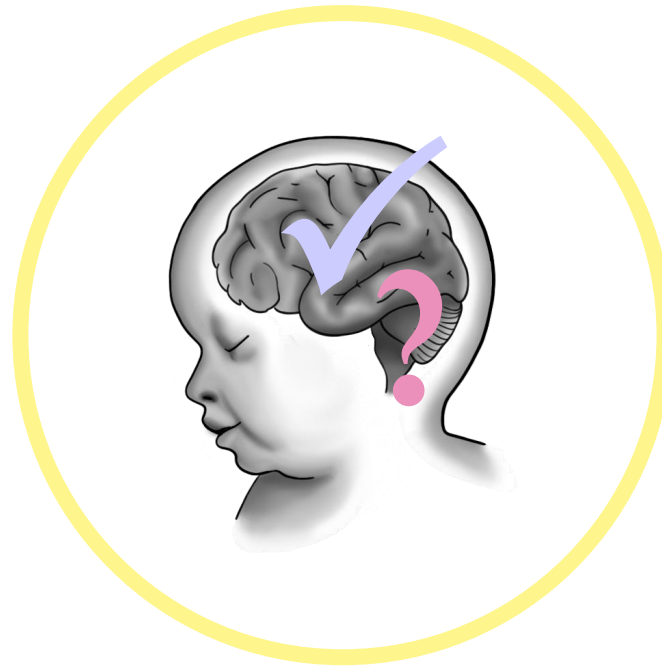
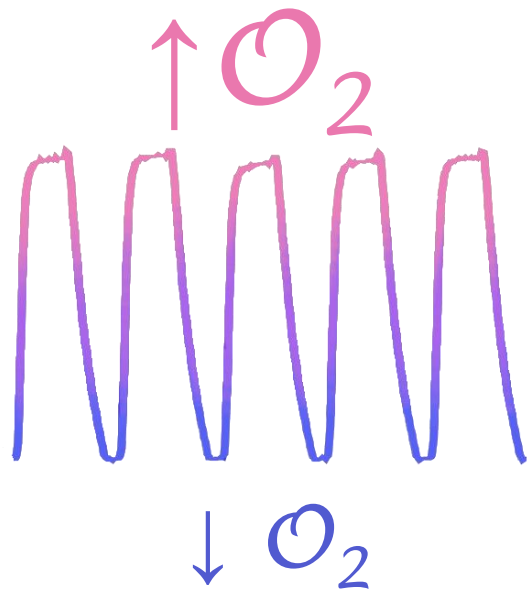
(Janvier *et al.*, 2004 ; Pillekamp *et al.*, 2007)

Epidemiology

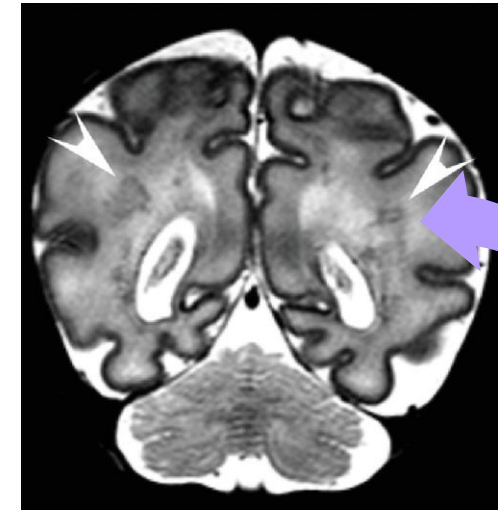


(Zhao *et al.*, 2011)

Intermittent Hypoxia and the Brain



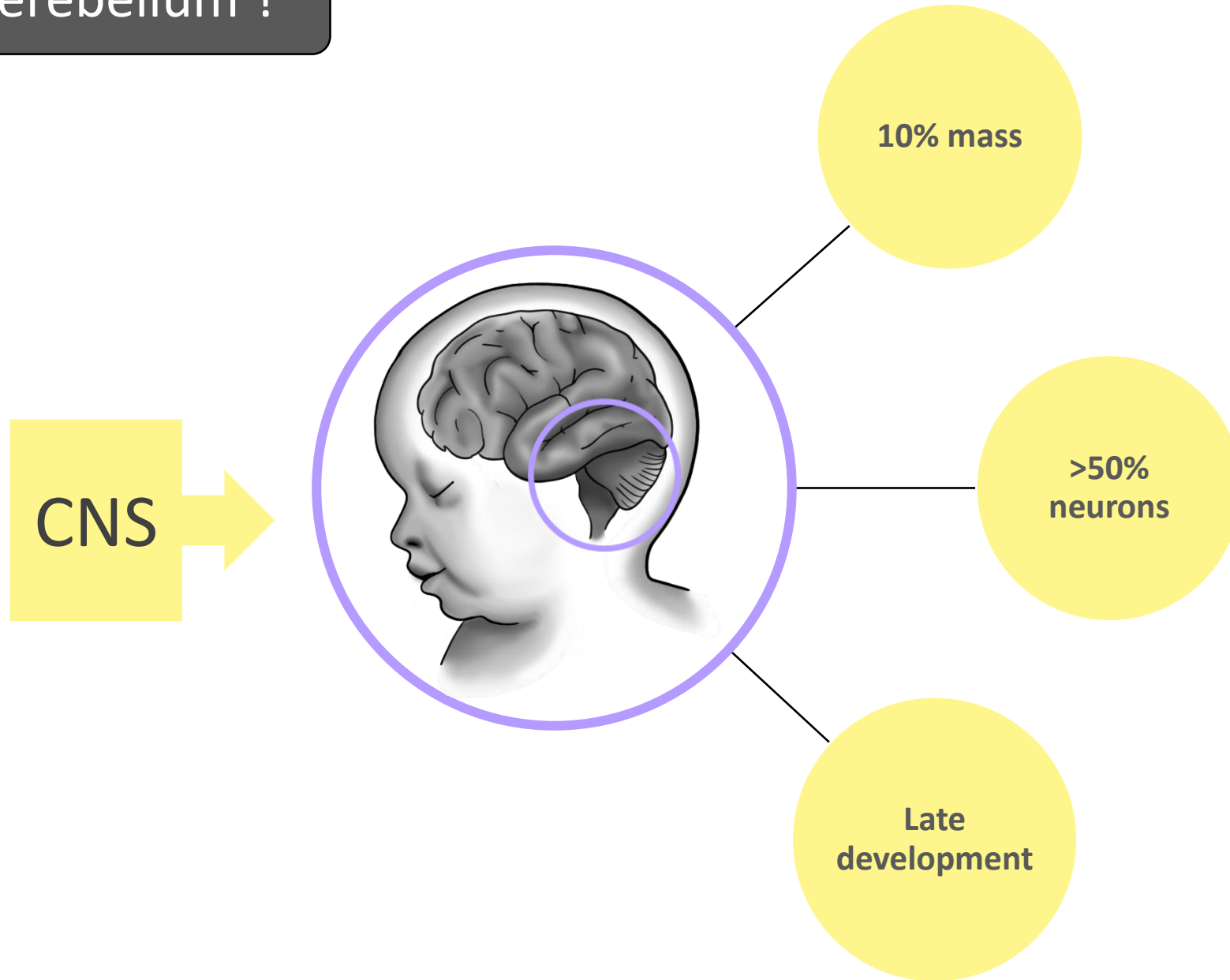
Anatomical
effects



(Van Bel *et al.*, 2019)

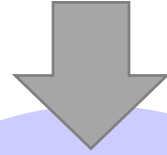
- Periventricular WM lesions
- Premature newborns

What is the Cerebellum ?



Importance of the Cerebellum

Immaturity
at birth



Motor
Skills

- Balance
- Coordination

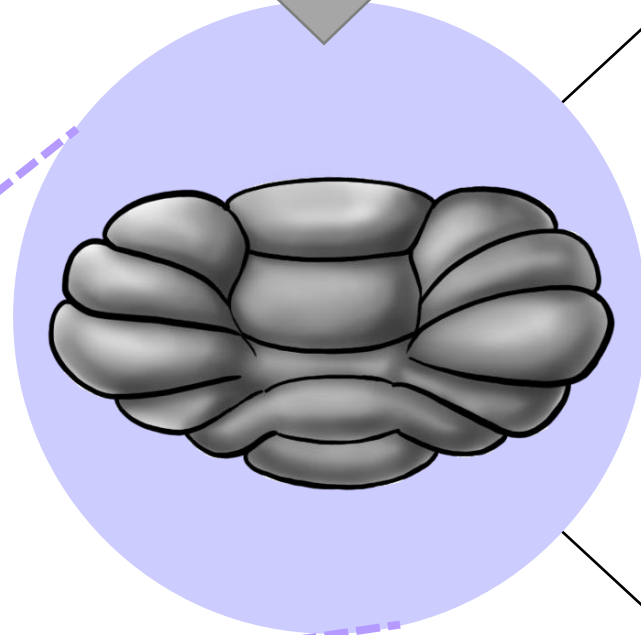
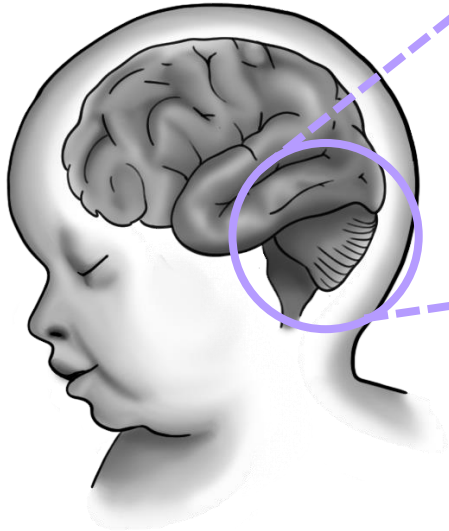
Cognition

- Attention
- Learning

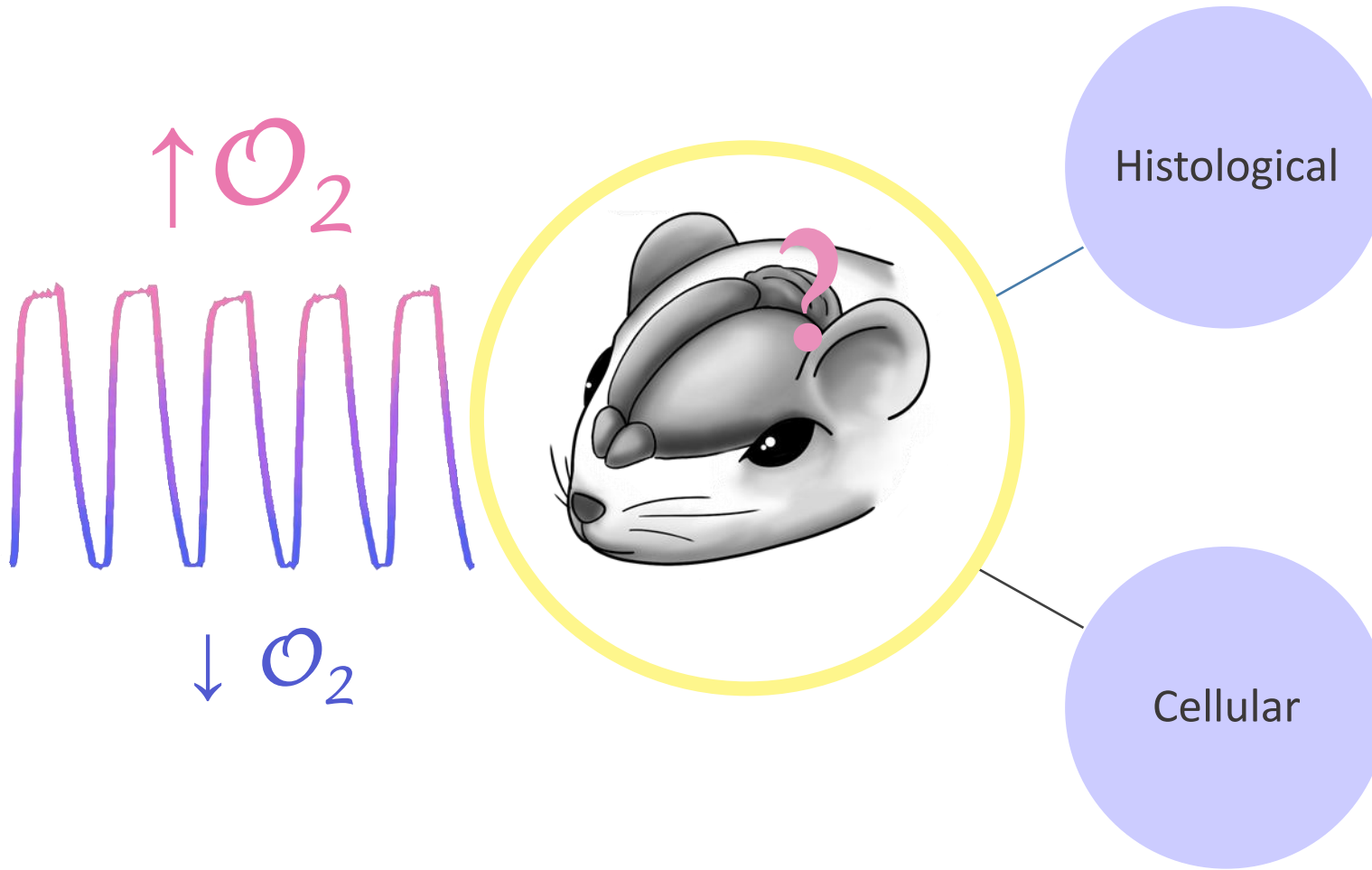
Behavior

- Affect
- Conduct

AoP



Intermittent Hypoxia and the Cerebellum

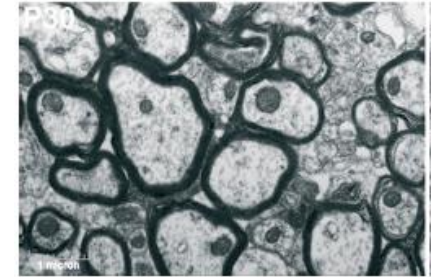


- Hypomyelination

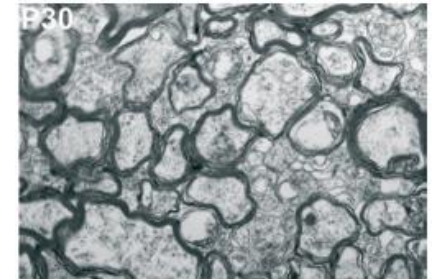
- Mouse

(Cai *et al.*, 2012)

Control



Intermittent Hypoxia



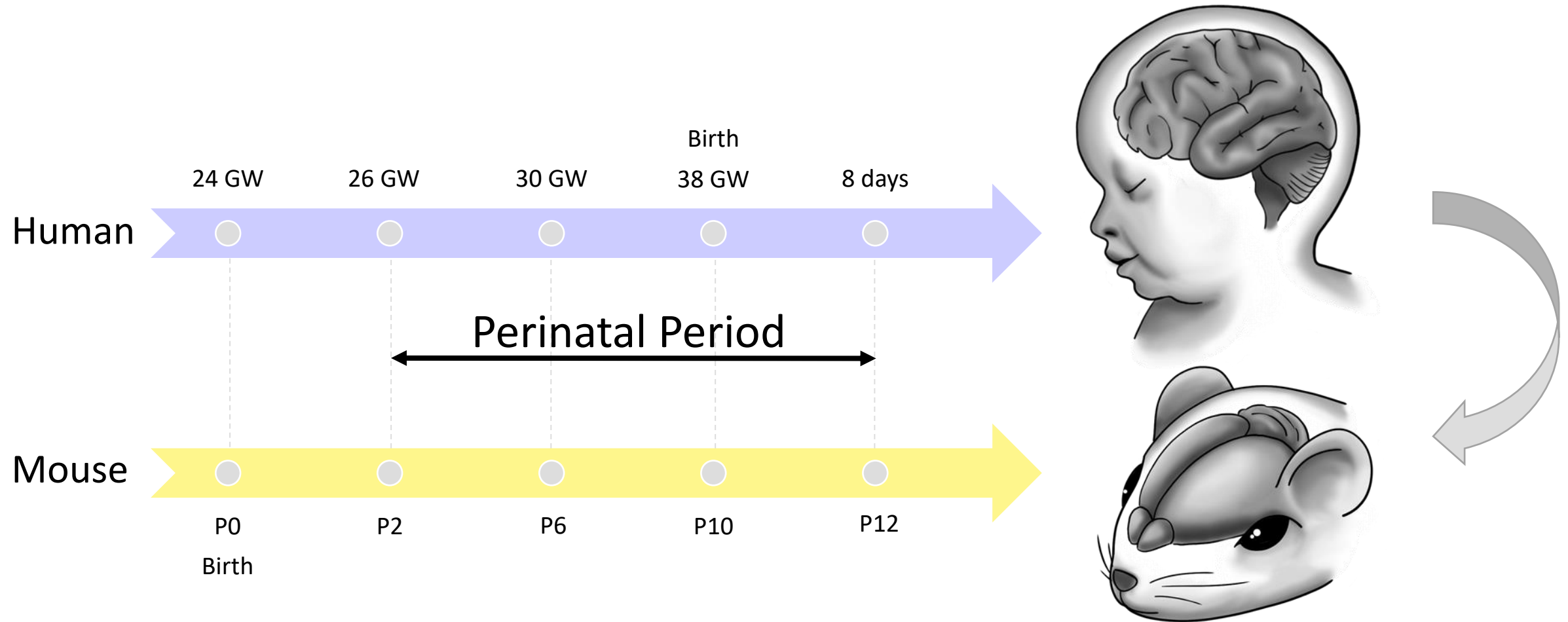
- \downarrow synaptic communication

- Mouse

(Goussakov *et al.*, 2019)

(Striatum - Cai *et al.*, 2012)

Model



Intermittent Hypoxia

Hypoxia/reoxygenation

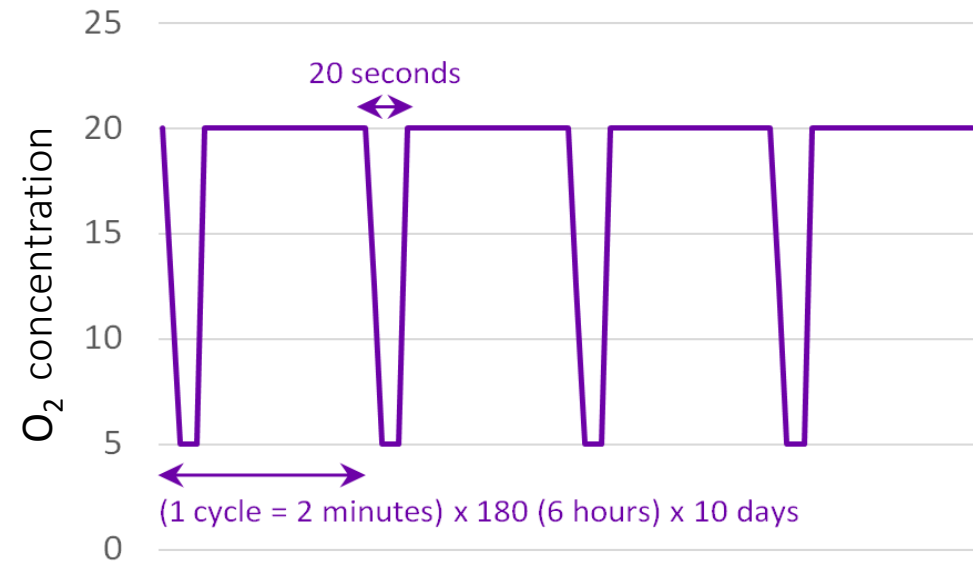
- 6 h/day, P2 → P12

1 cycle

- 2 min with 20 seconds at 5% O₂

Environment

- Same for controls



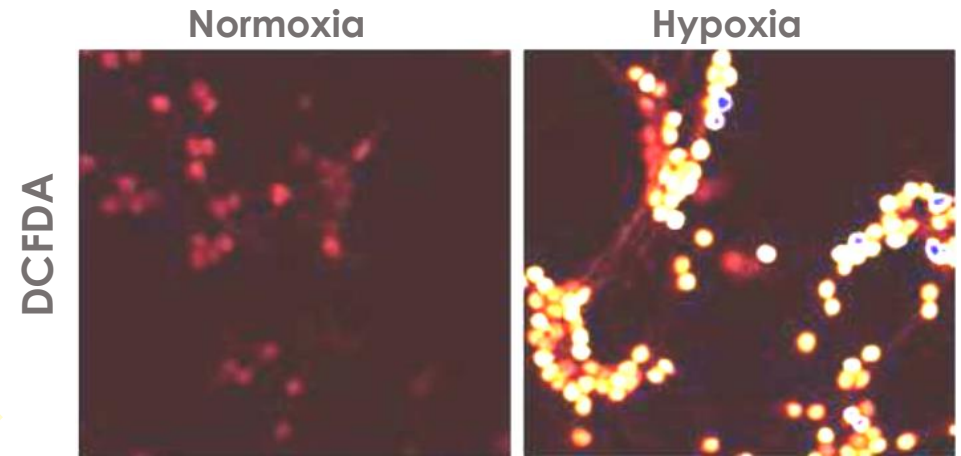
Model of Apnea of Prematurity

Intermittent Hypoxia causes Oxidative Stress

↑ROS
In vitro

- Granule cell culture
- Rat P7

(Chiu *et al.*, 2012)

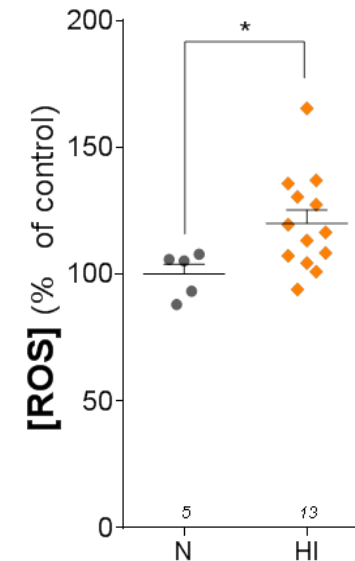


(Chiu *et al.*, 2012)

↑ROS
In vivo

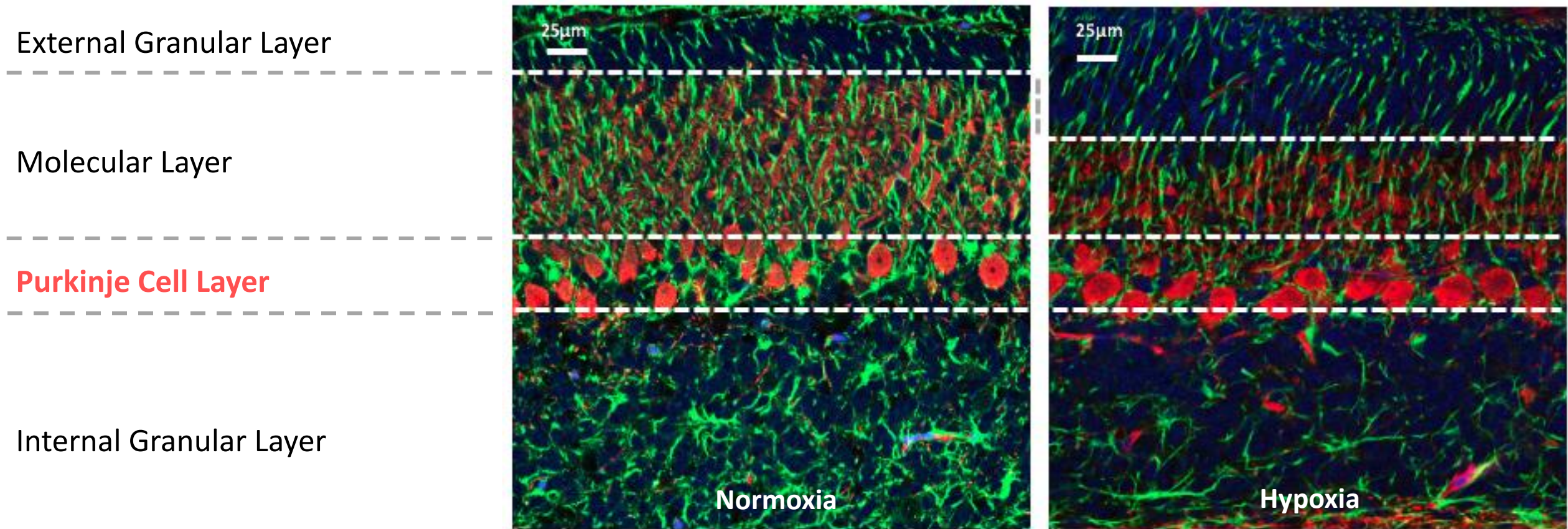
- Whole cerebellum
- Mouse P12

(Leroux *et al.*, in preparation)



(Leroux *et al.*, in preparation)

Layers of the Cerebellum



(Leroux *et al.*, in preparation)

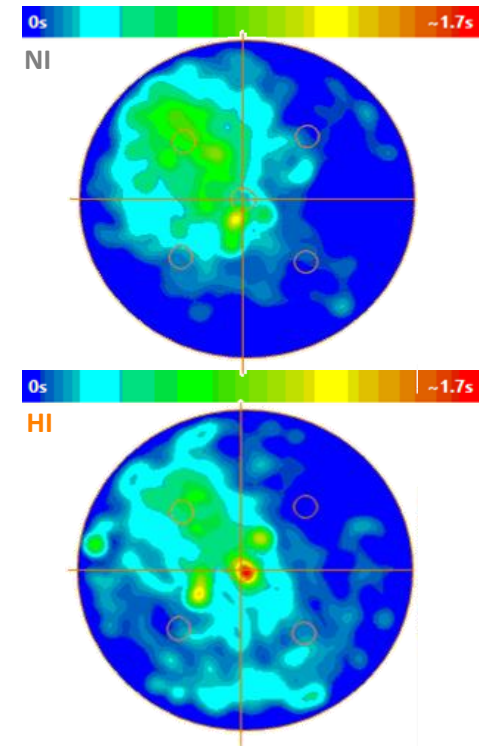
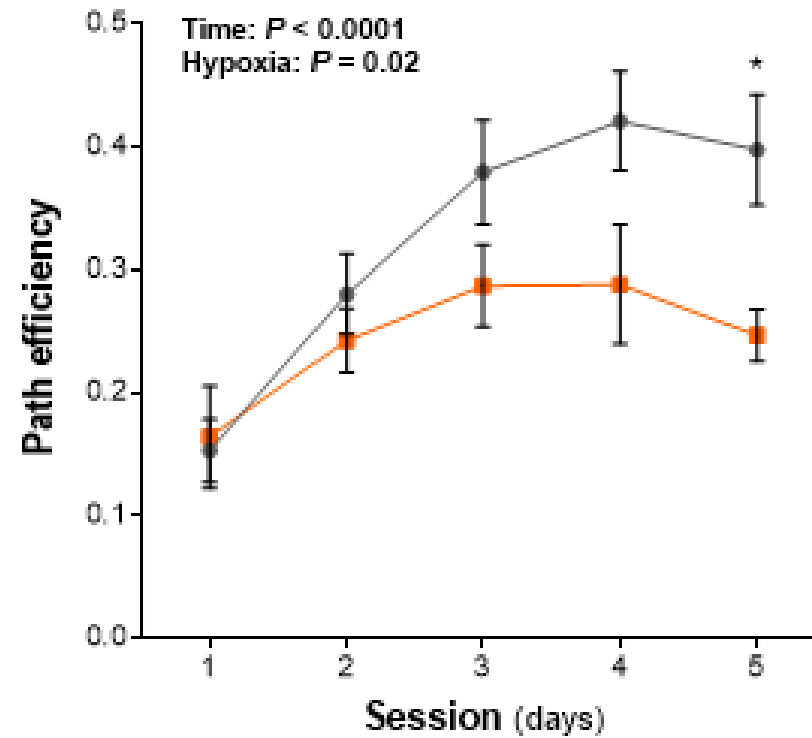
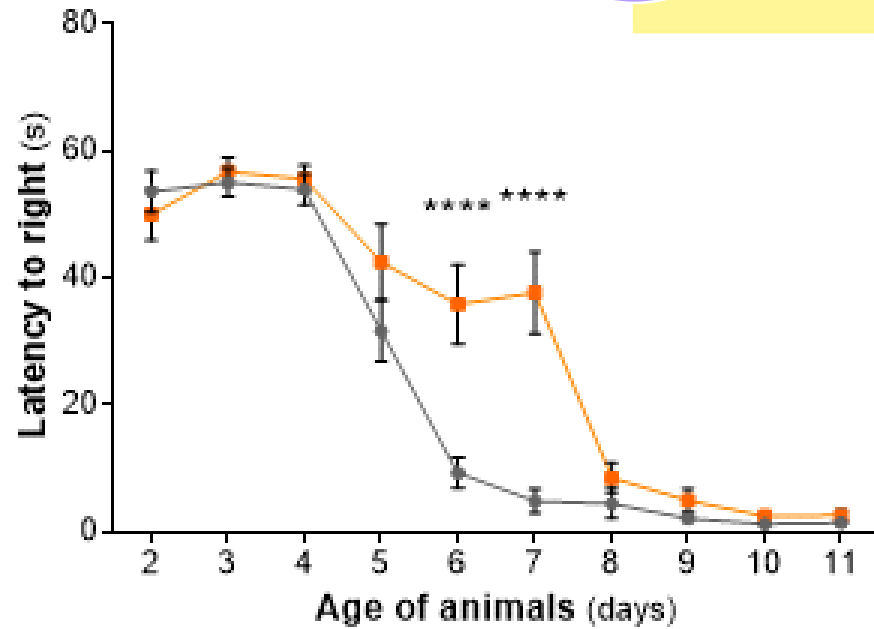
Behavioral Tests

Pups

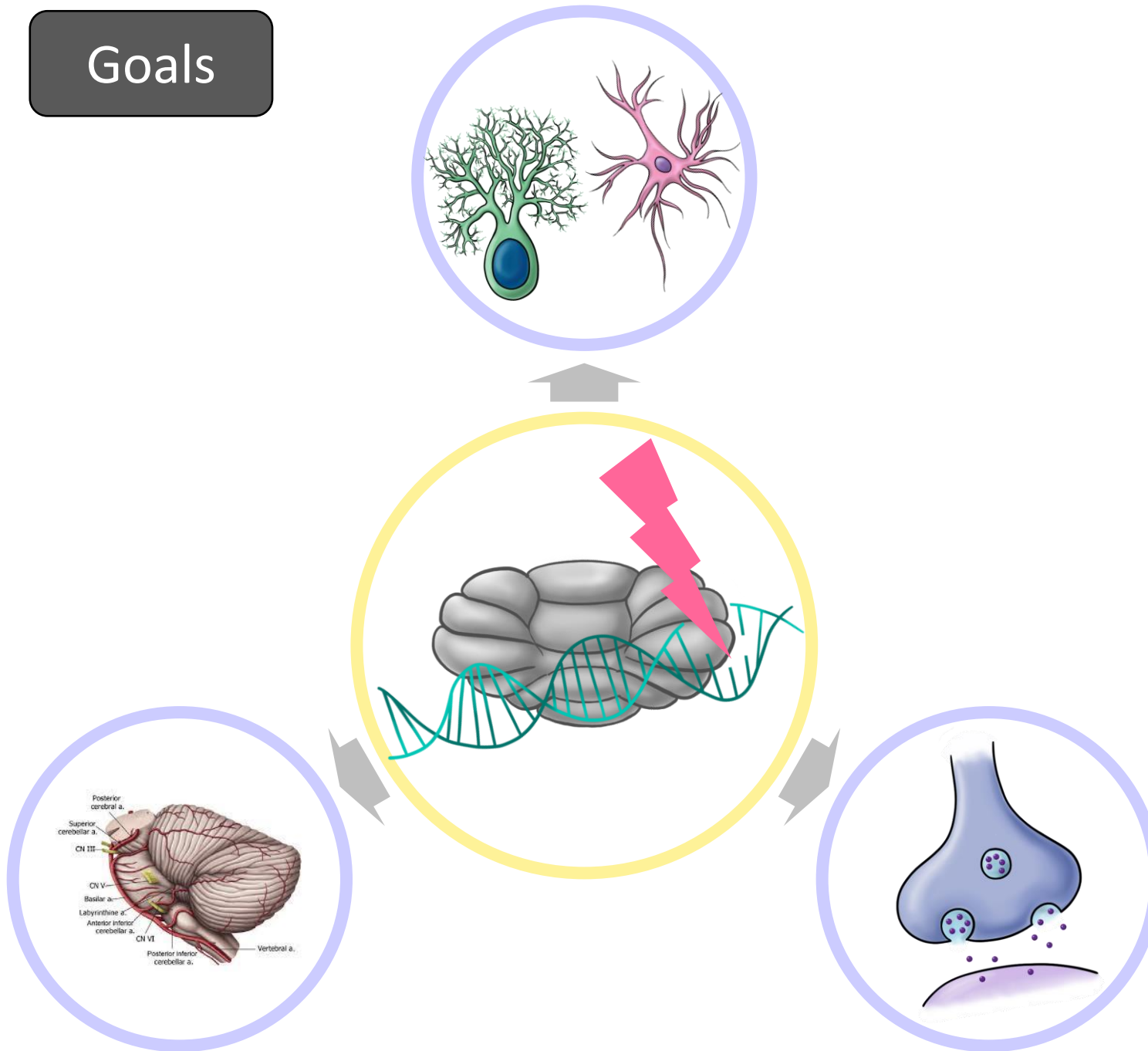
- Slower to get upright
- Lower coordination

Adults

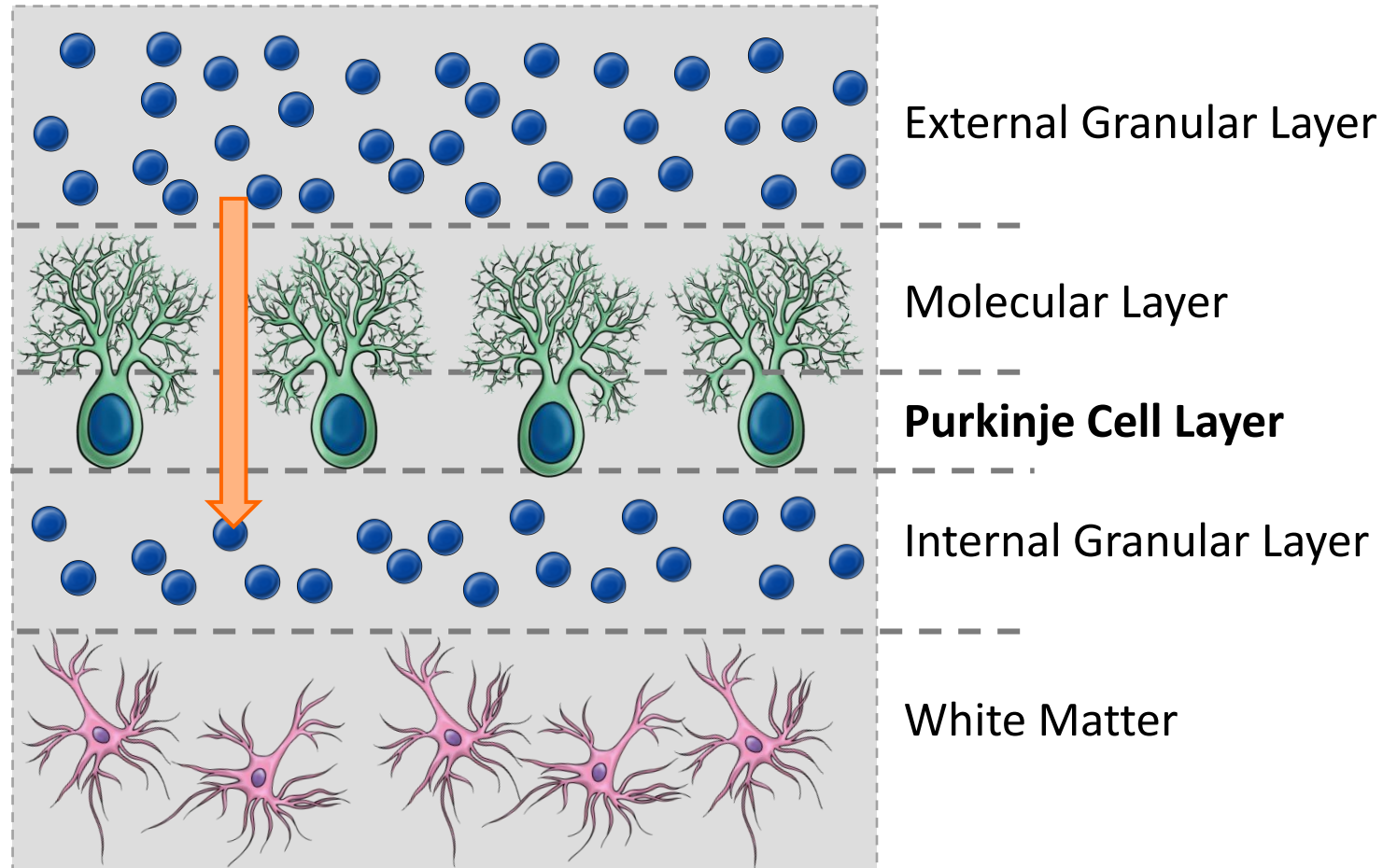
- Less efficient direction
- Meandering in the pool



Goals



Layers of the developing cerebellar cortex



P4

P8

P12

P21

Methods

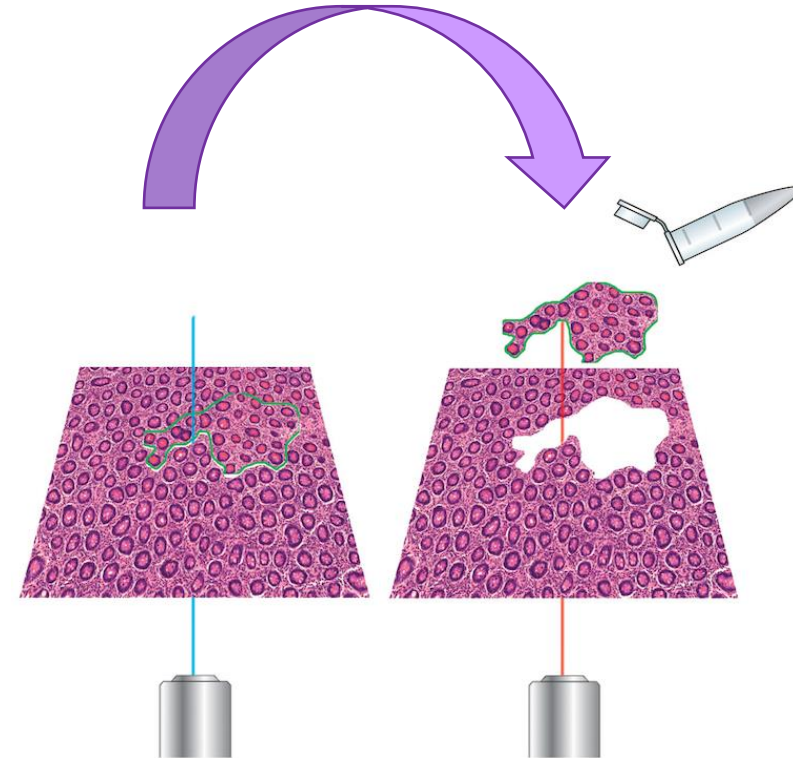
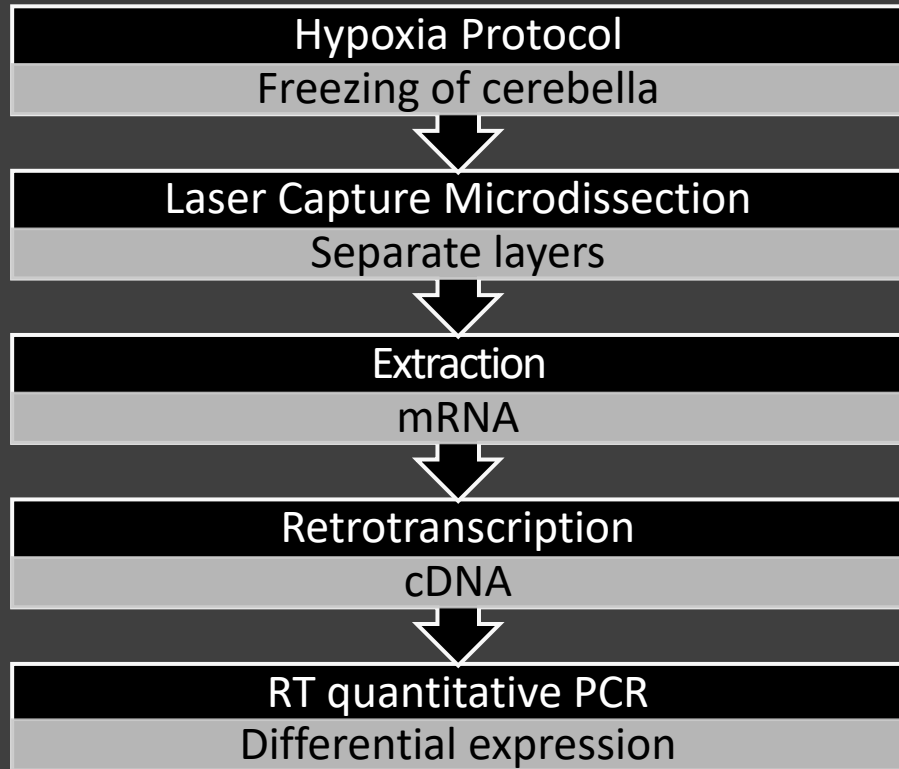
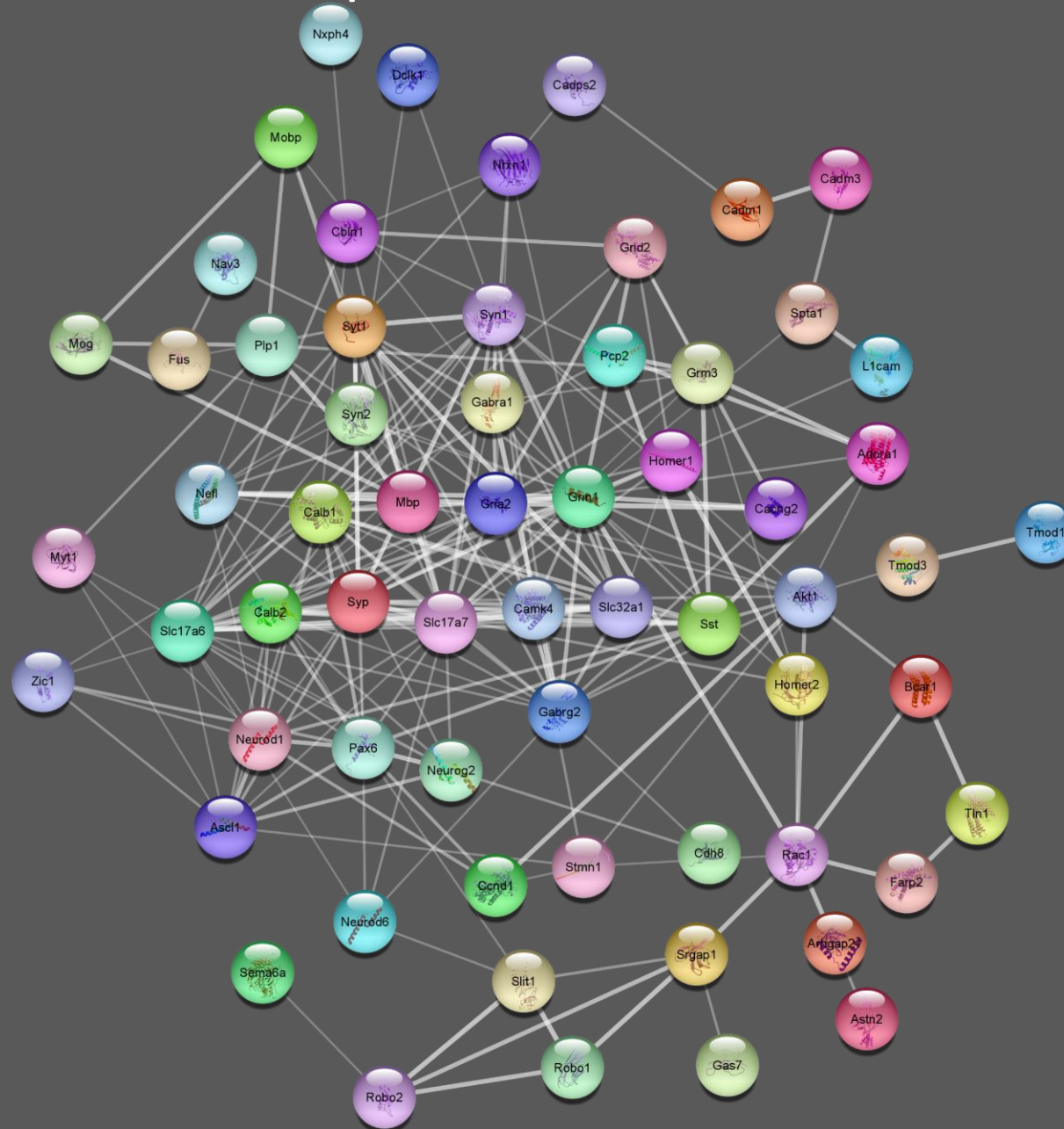
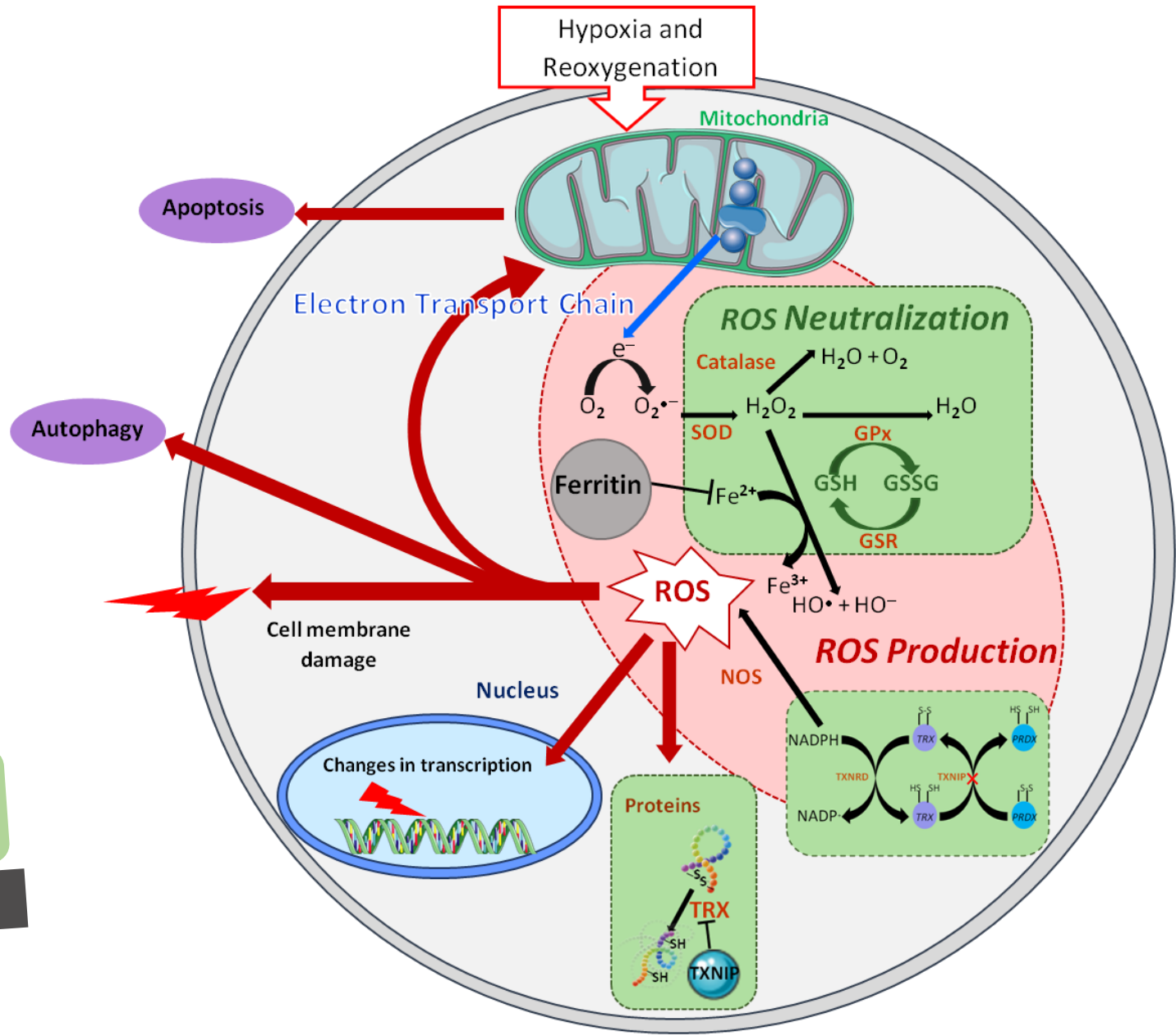
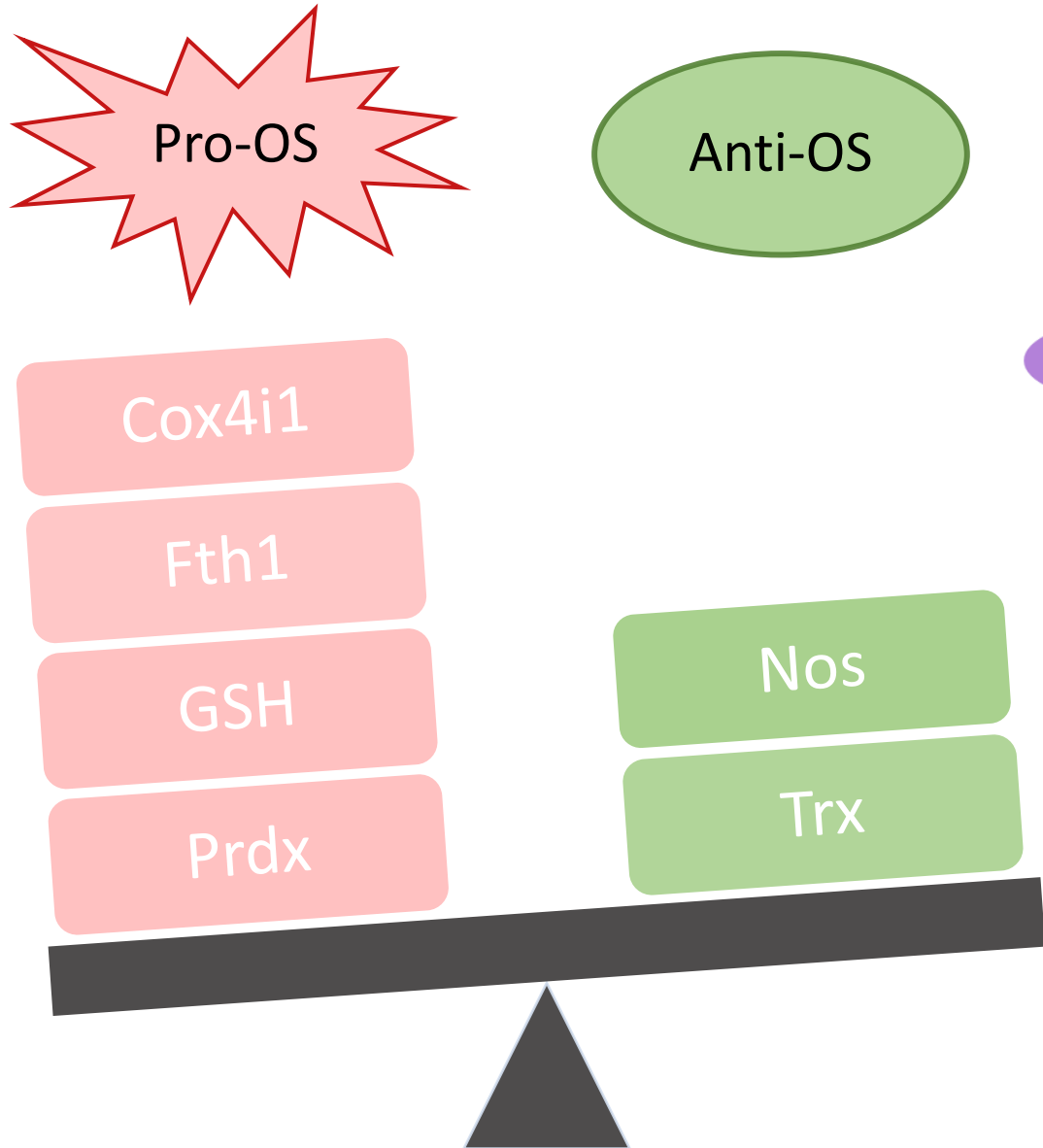


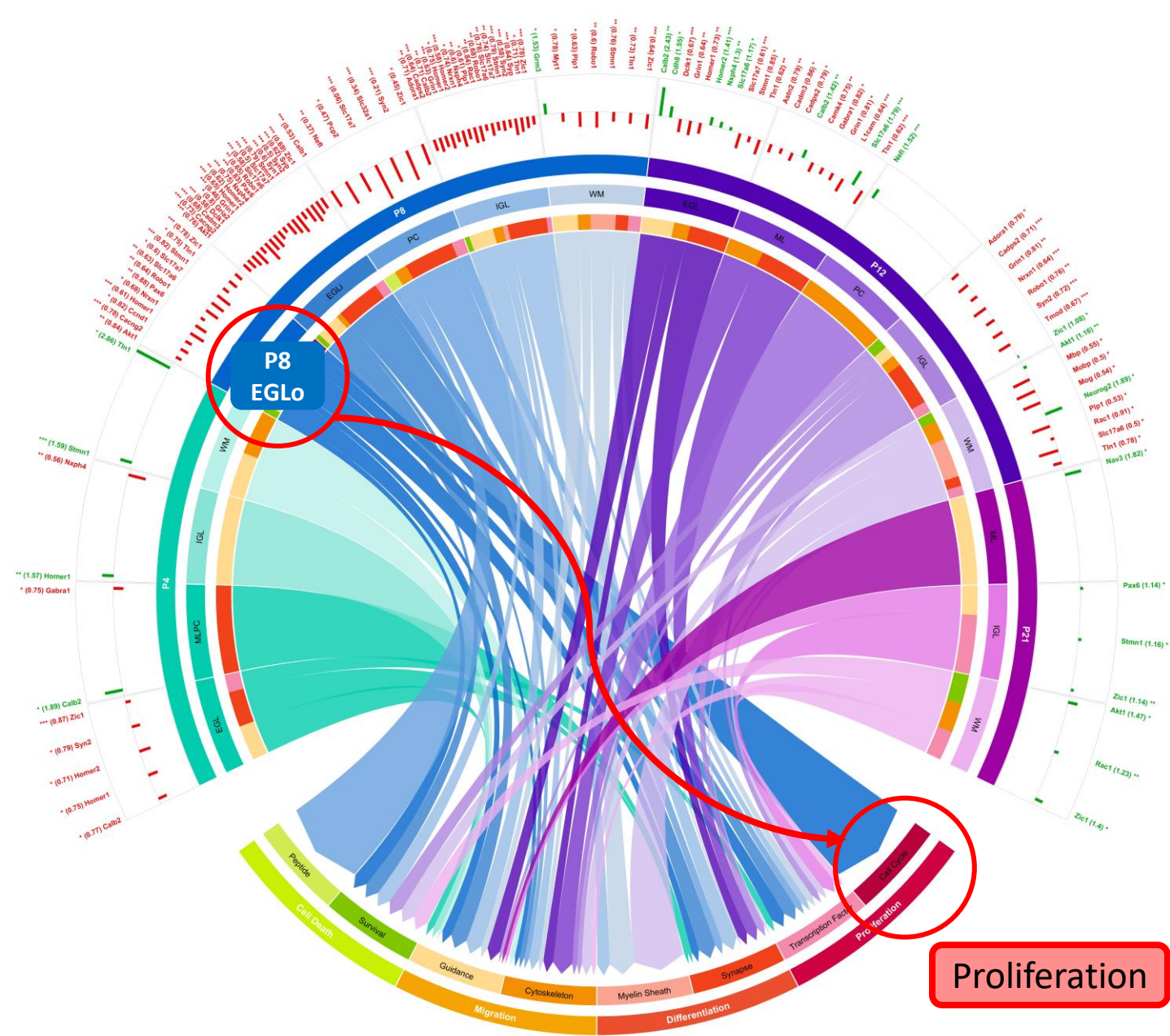
Image rights: University of Copenhagen

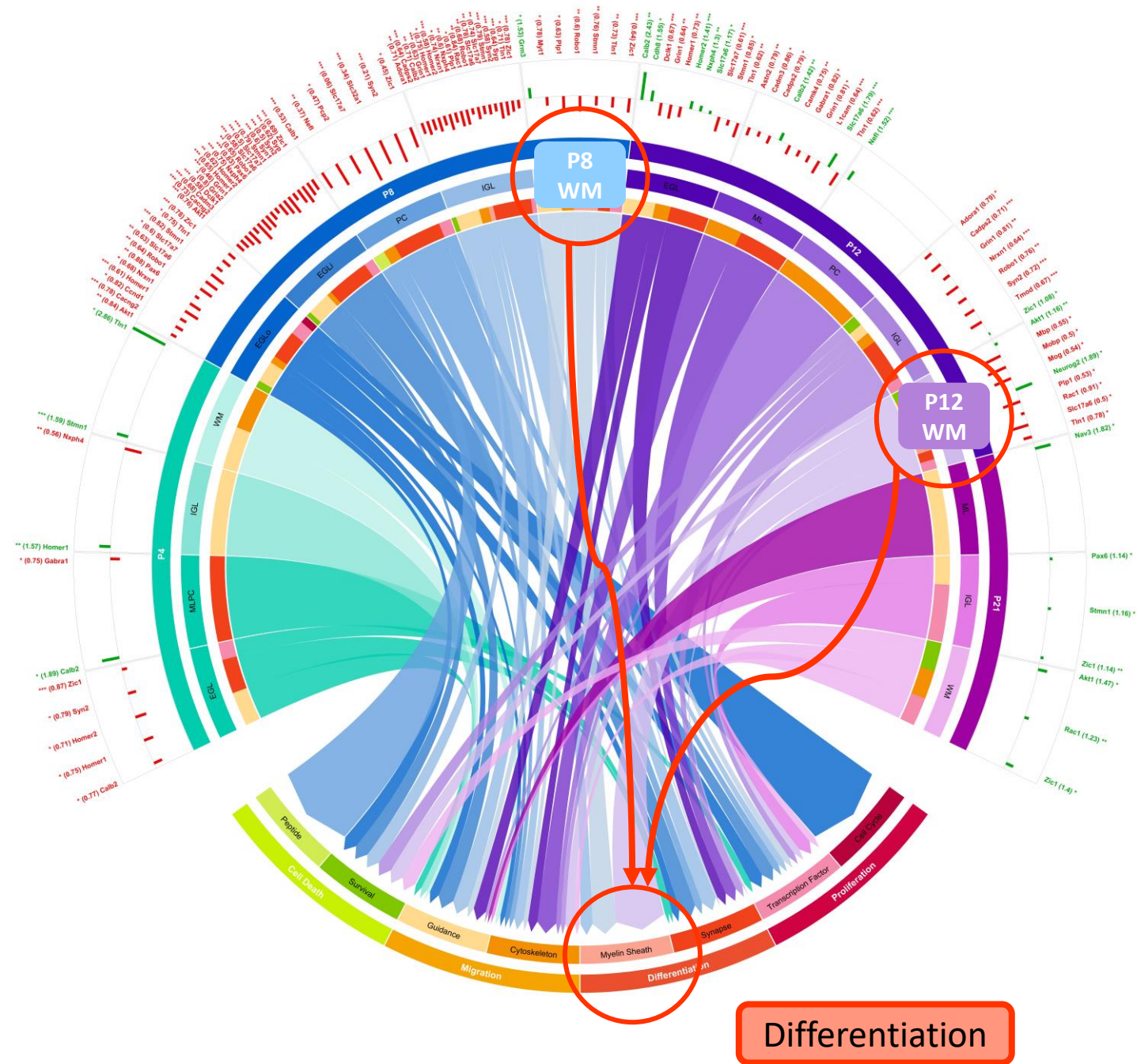
Development Gene Set



Oxidative Stress (OS)

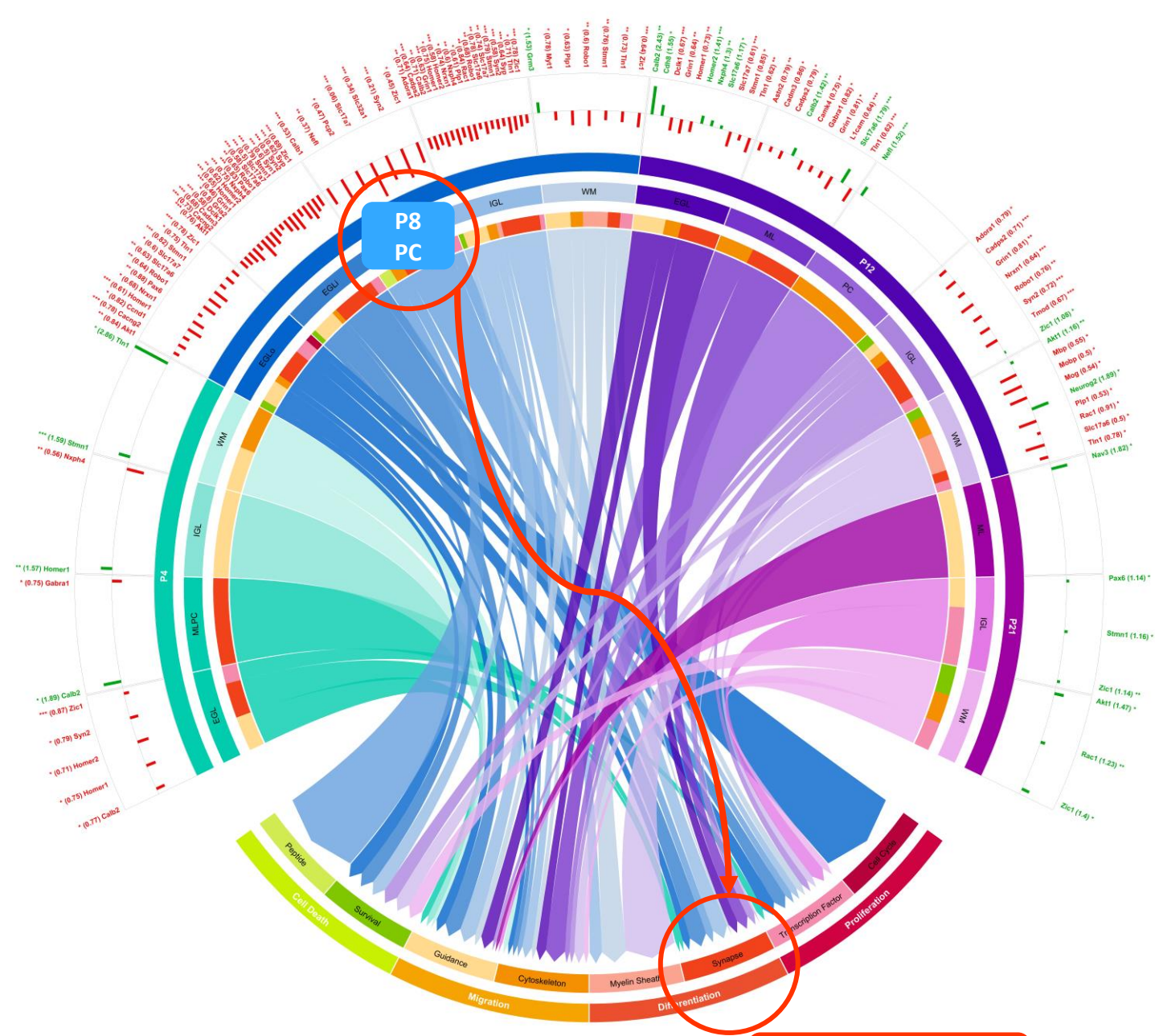






Differentiation

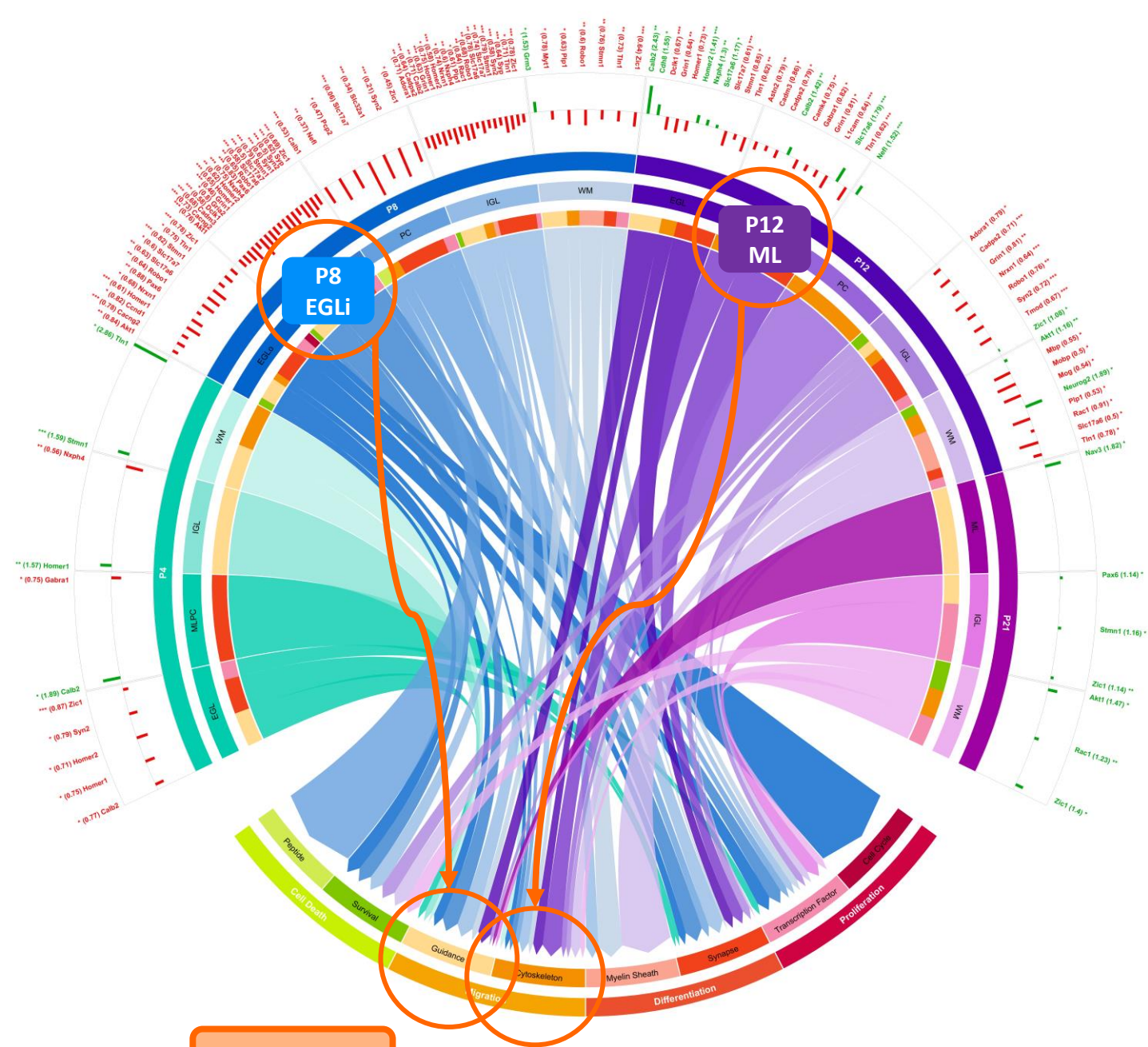
Hypoxia influence on gene expression



Differentiation

Hypoxia influence on gene expression

(Rodriguez-Duboc *et al.*,
in preparation)

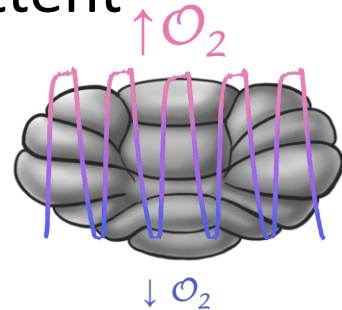


Migration

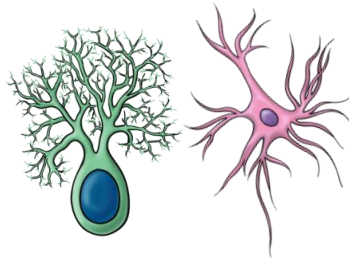
Hypoxia influence on gene expression

Consequences

Intermittent Hypoxia

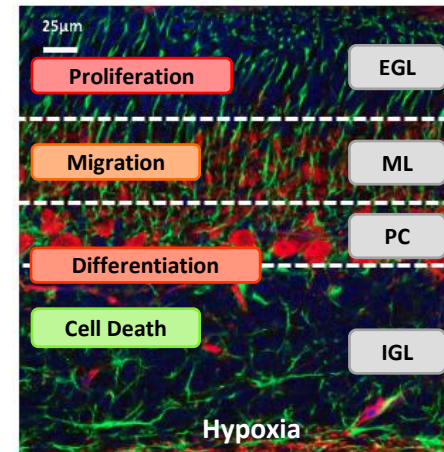


Cell Phenotype and Activity

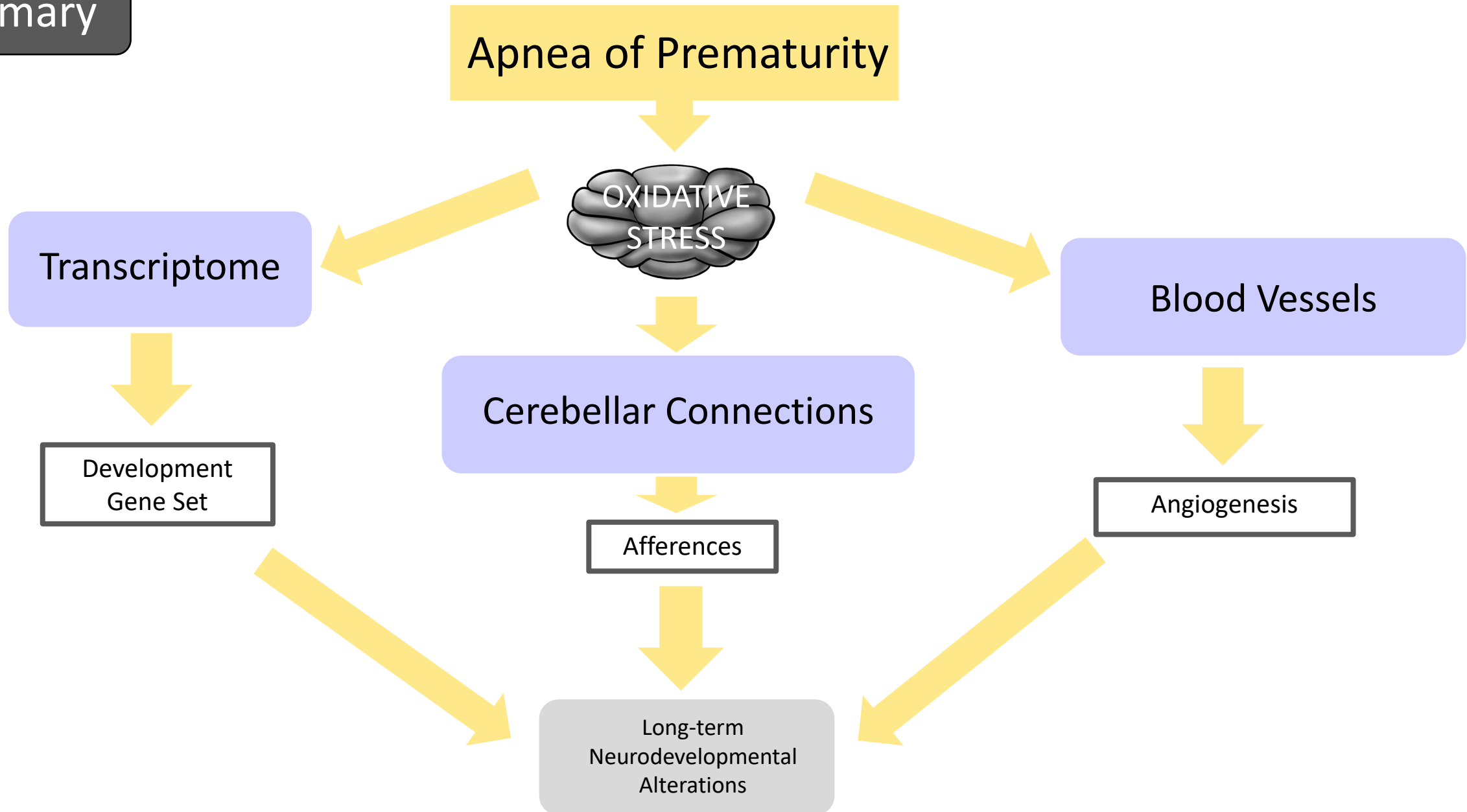


Histological Defects

Behavioral Deficits



Summary





Questions?

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MINISTÈRE DE L'ENSEIGNEMENT
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L'INNOVATION

