

Linking early development with neuronal circuit outcome

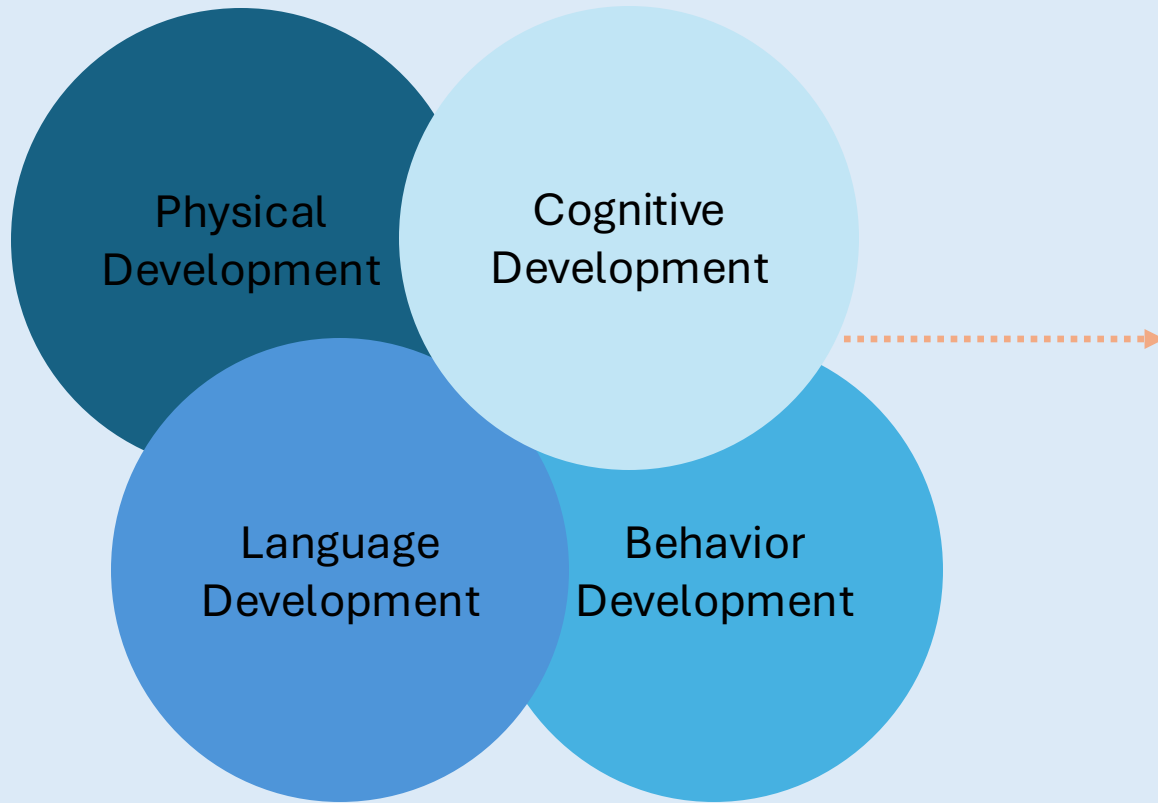
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The key to treat developmental brain disorders

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University Medical Centre Utrecht, The Netherlands

Developmental Disorders

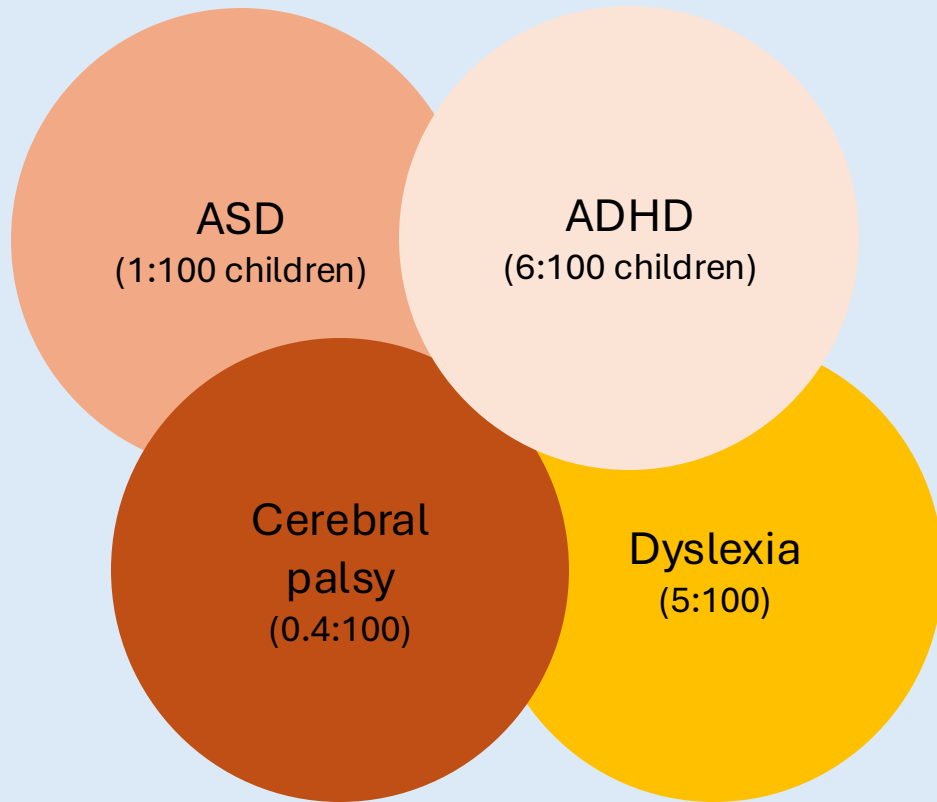


Limitations in the daily functioning of millions of children

Long lasting conditions

Significant impact on health, education and economy

Brain developmental disorders



Challenges

Complexity and variability of the symptoms

Lack or insufficient biomarkers

Limited treatment options

Variability in treatment responses

Enigmatic

Limitations in understanding
its development

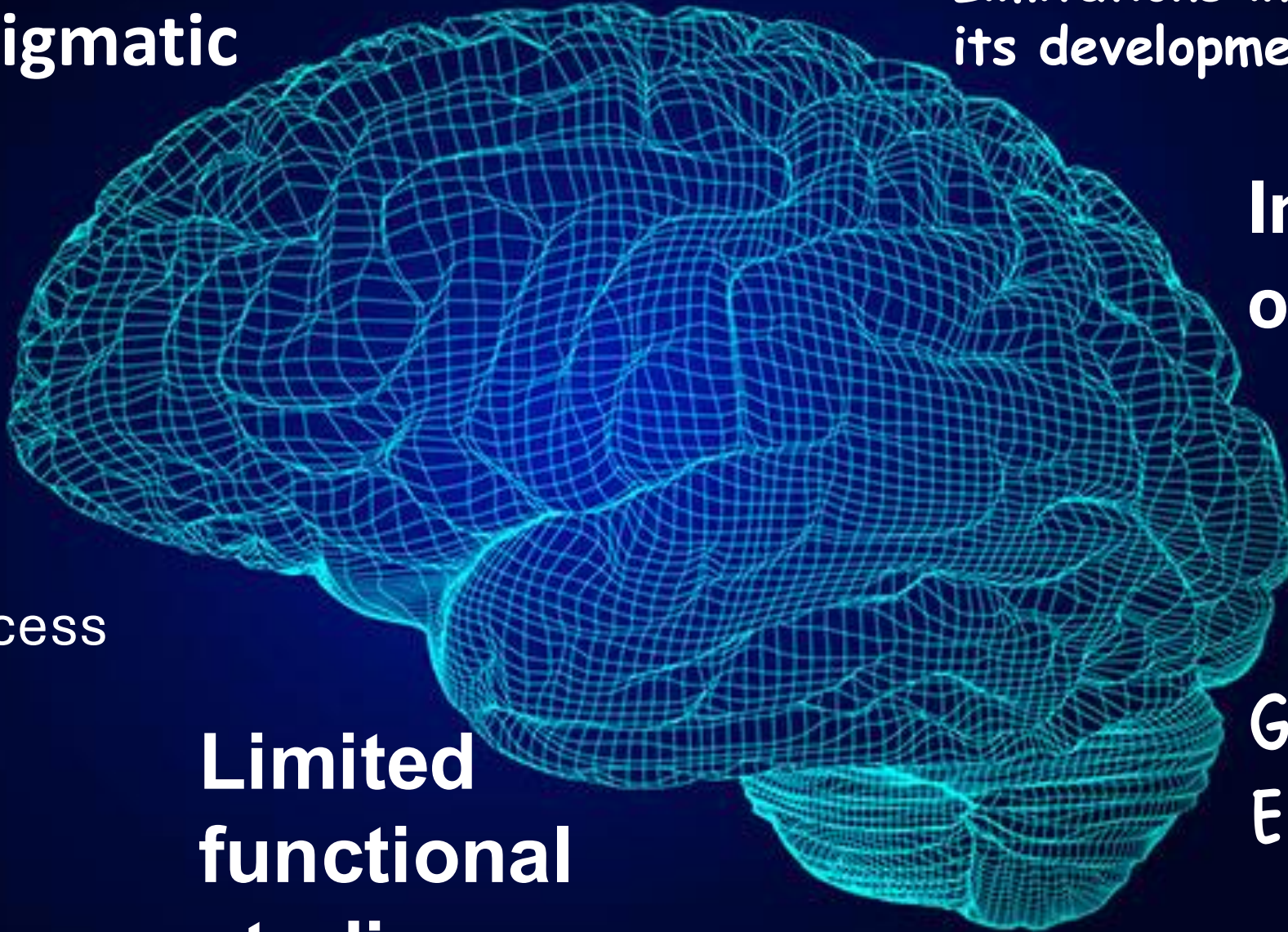
**VARIATIONS
ACROSS AGE**

**Influence
of lifestyle**

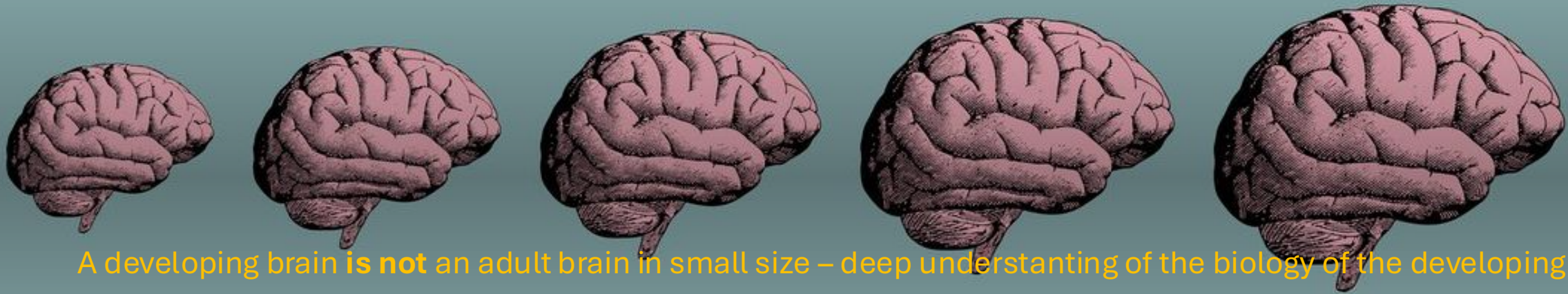
Limited access

**Limited
functional
studies**

**Genes *vs.*
Environment**



Linking early development with neuronal circuit outcome



A developing brain **is not** an adult brain in small size – deep understanding of the biology of the developing brain

Identify pathways and time windows to restore neuronal circuit function (clinics)

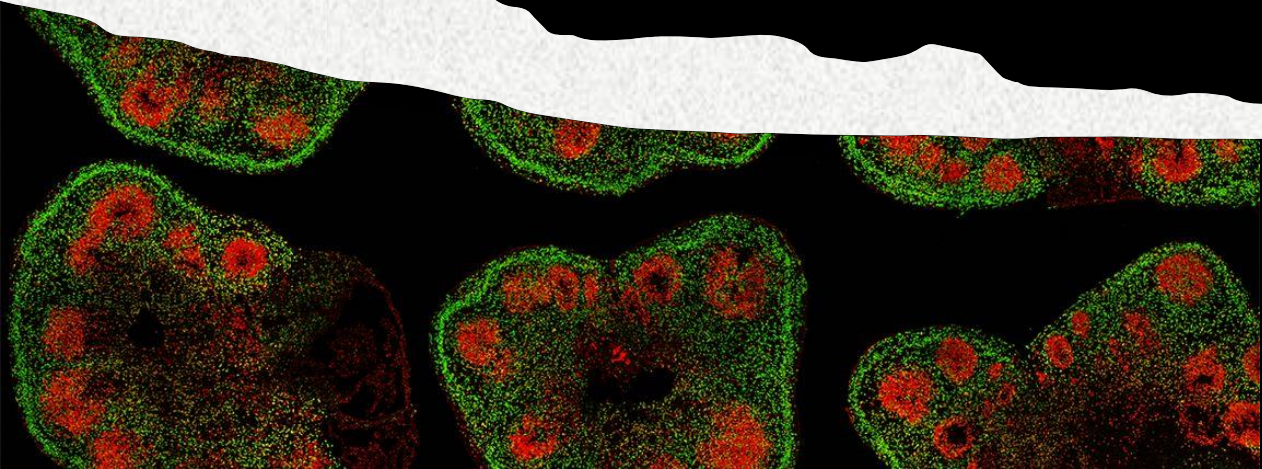
Models must allow to **establish causality** between early perturbations and late circuit function

Test therapies

Follow up overtime

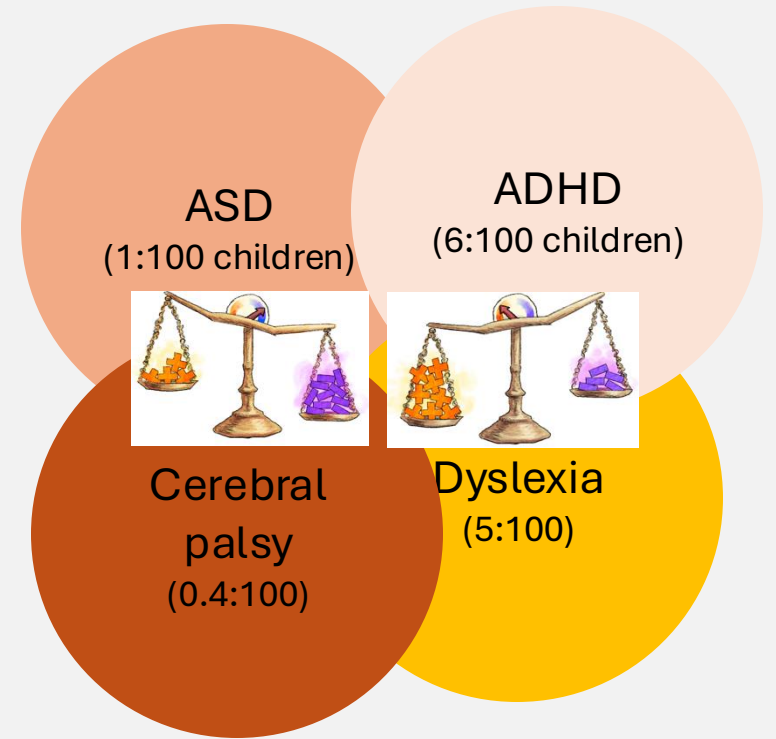


Good models to study the human brain and human developmental diseases

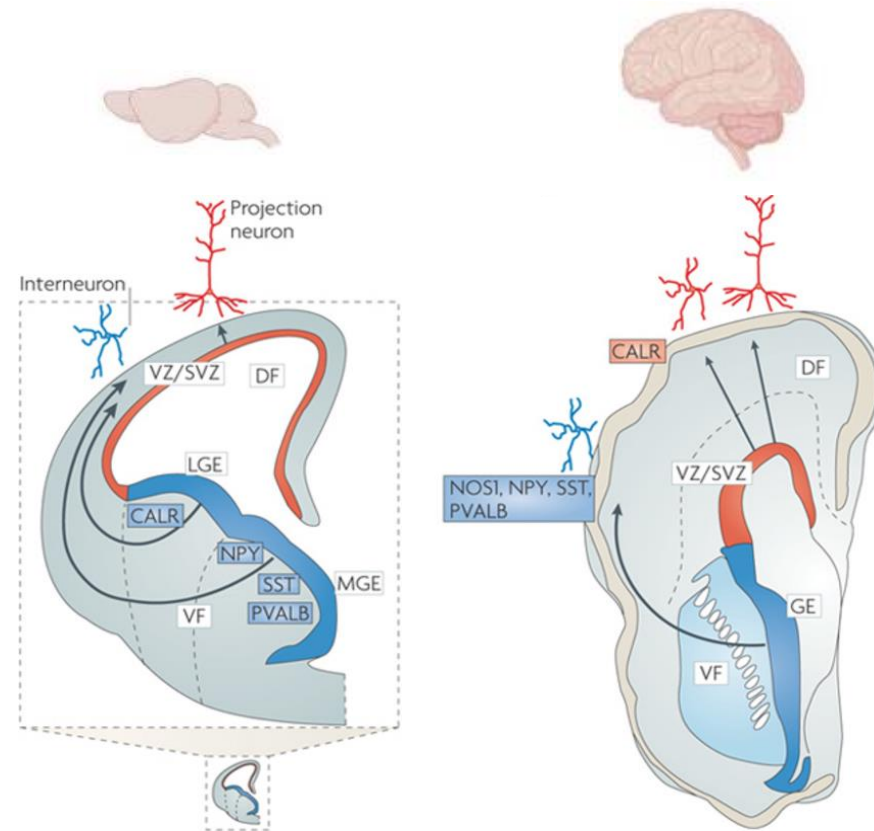


The focus of my research

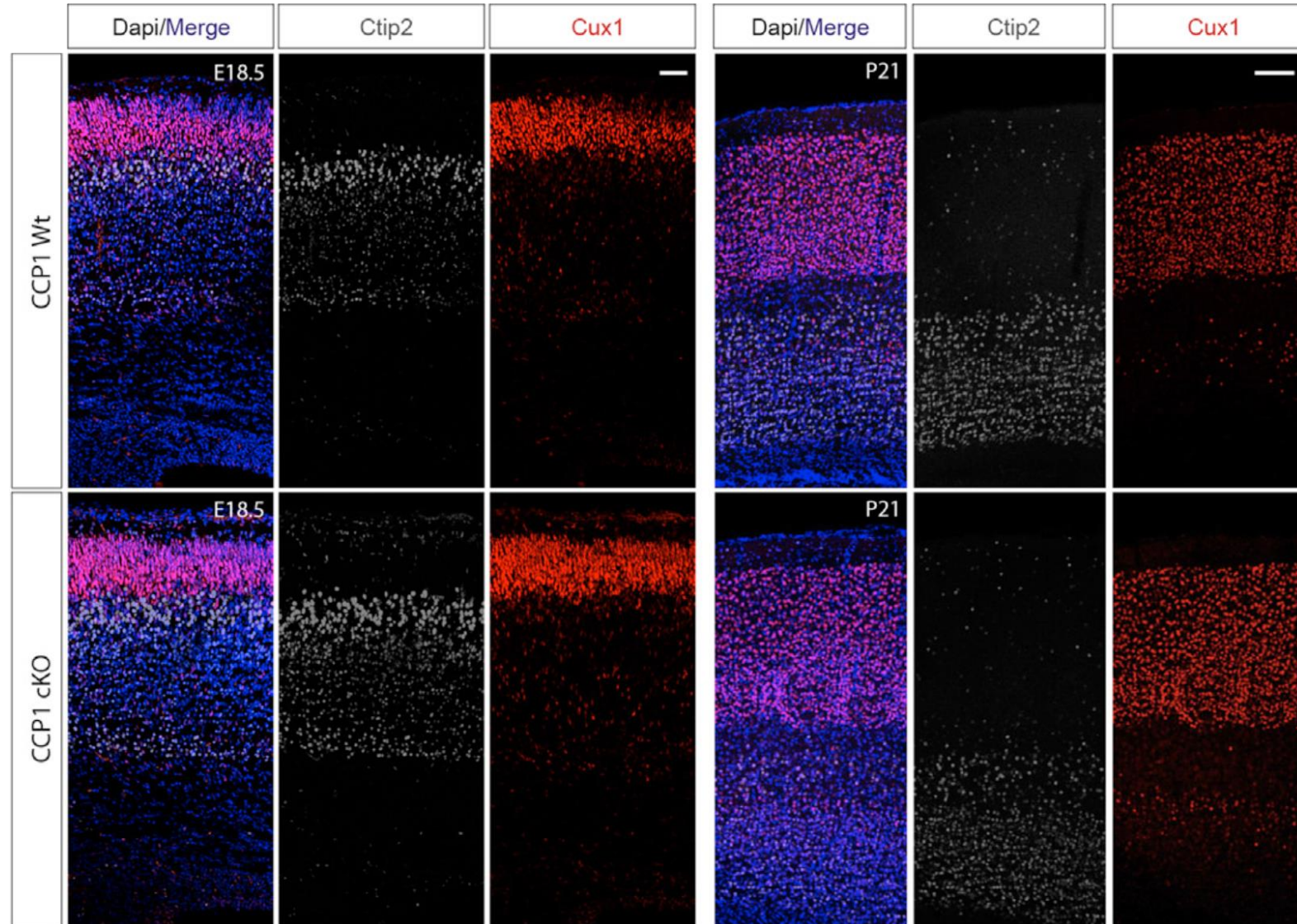
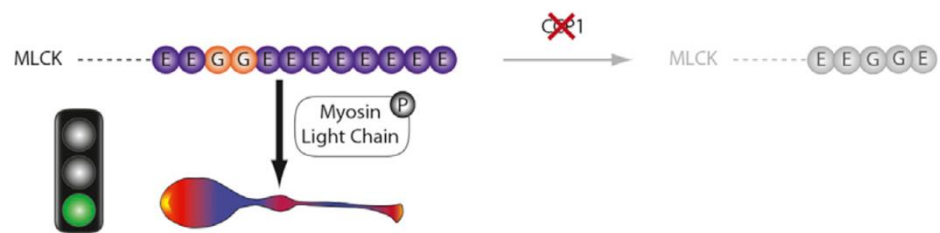
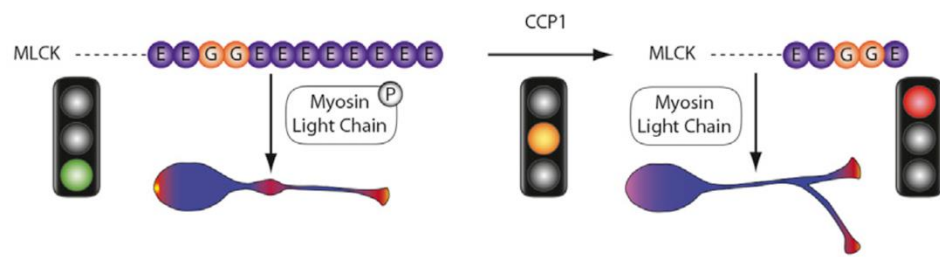
The inhibitory system



New mechanisms uncovering the formation of neuronal circuits – role of interneuron dynamics

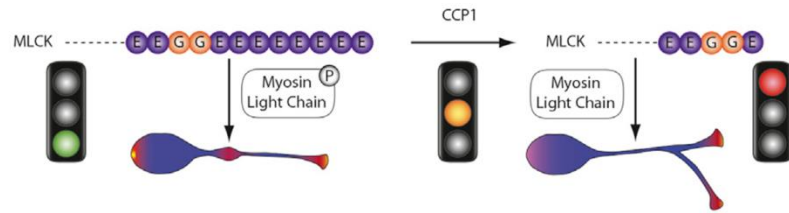


New mechanisms uncovering the formation of neuronal circuits – role of interneuron dynamics



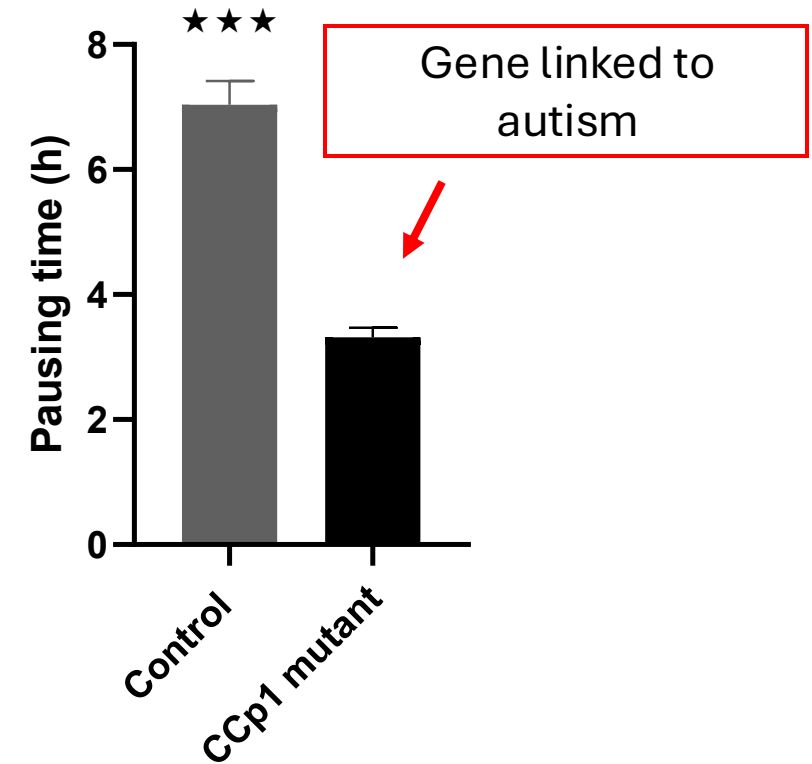
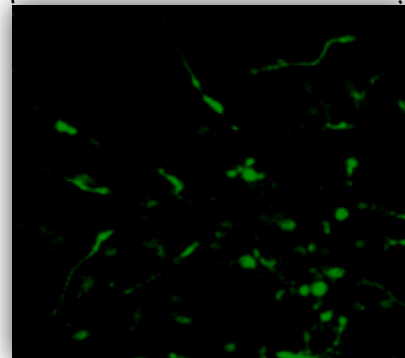
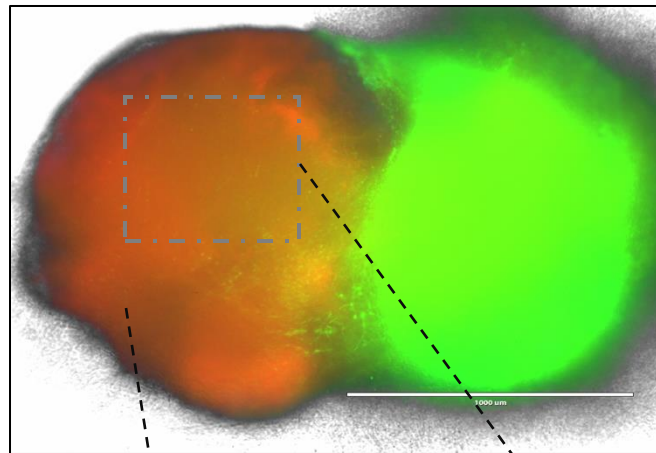
New mechanisms uncovering the formation of neuronal circuits – role of interneuron dynamics

Human Context



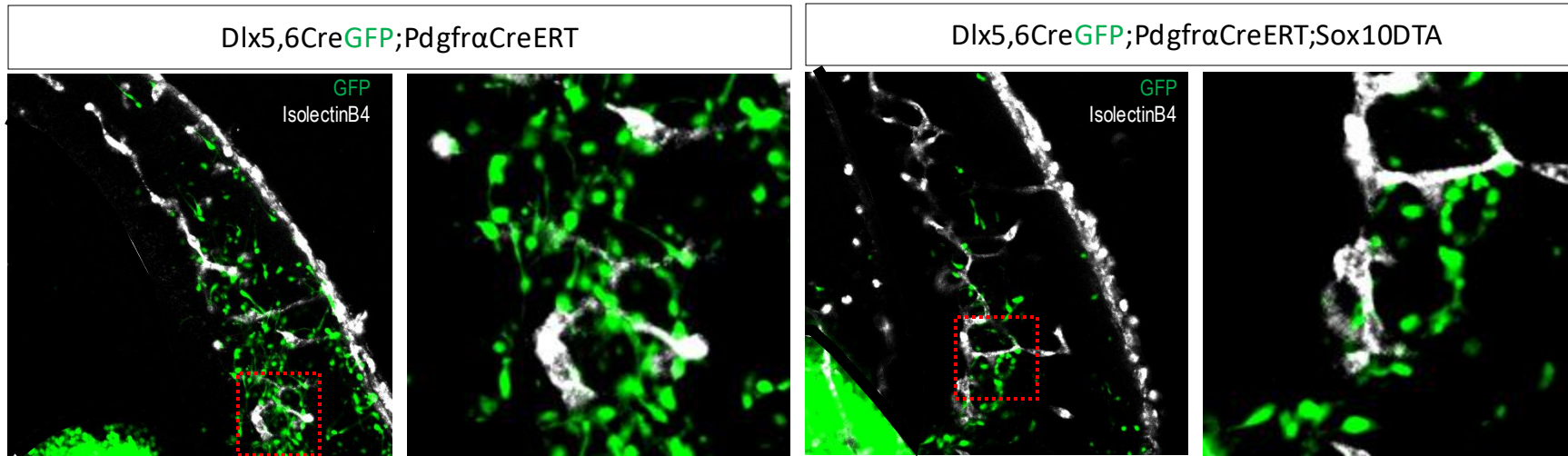
Dorsal

Ventral

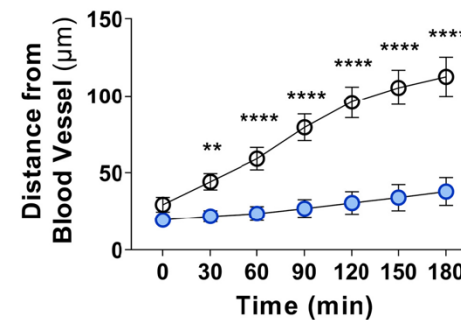
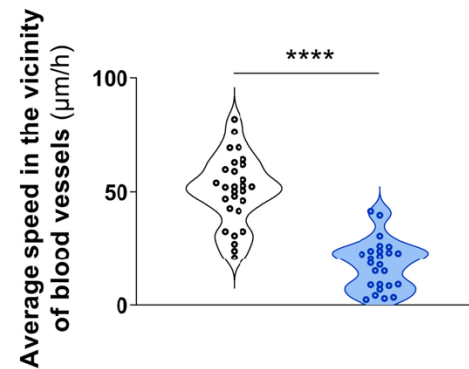


New mechanisms uncovering the formation of neuronal circuits – role of neural cells with atypical functions

Interneurons; Blood Vessels



OPC Depletion

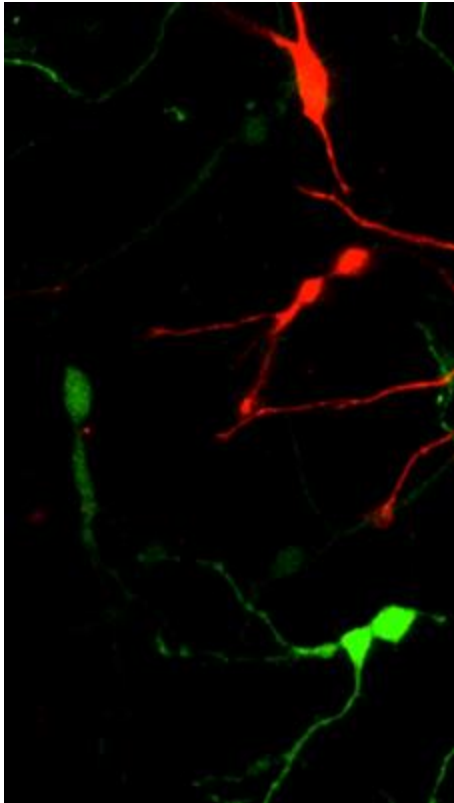


- ⊖ GFP⁺cINs-control
- GFP⁺cINs-OPC-depleted

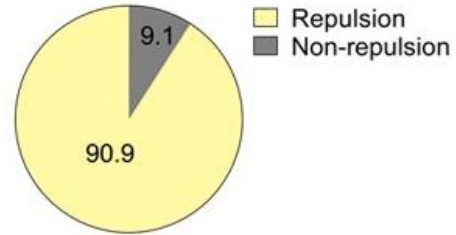
New mechanisms uncovering the formation of neuronal circuits – role of neural cells with atypical functions

Red: Interneuron

Green: OPC



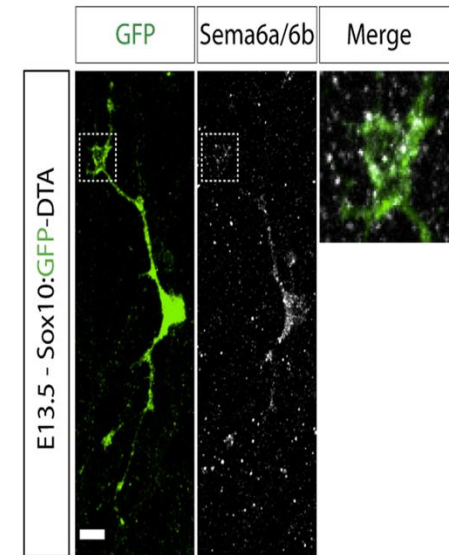
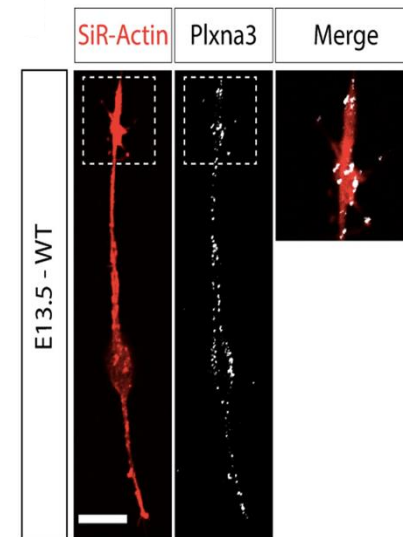
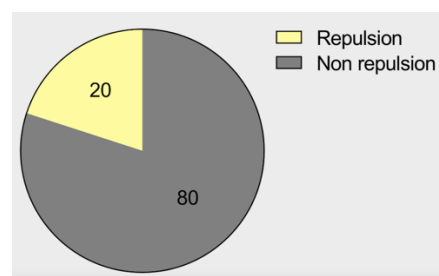
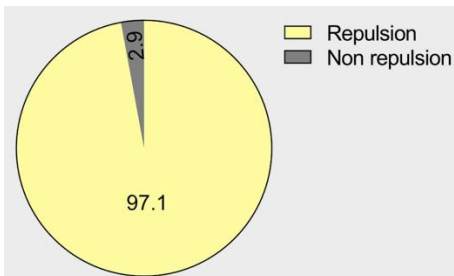
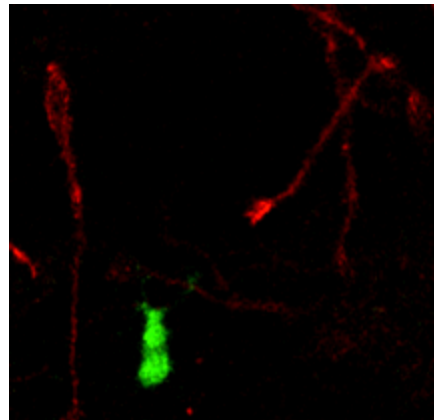
Sema6B

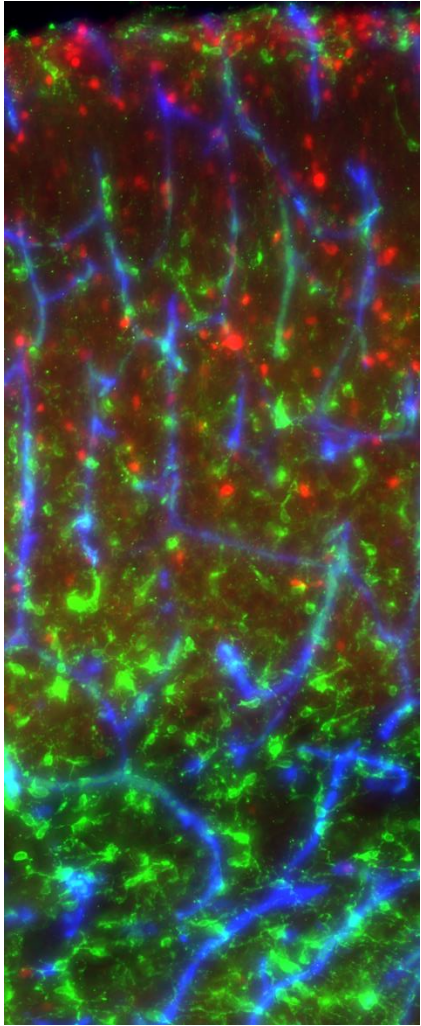


Red: Interneuron

Green: OPC

siRNA PlexinA3





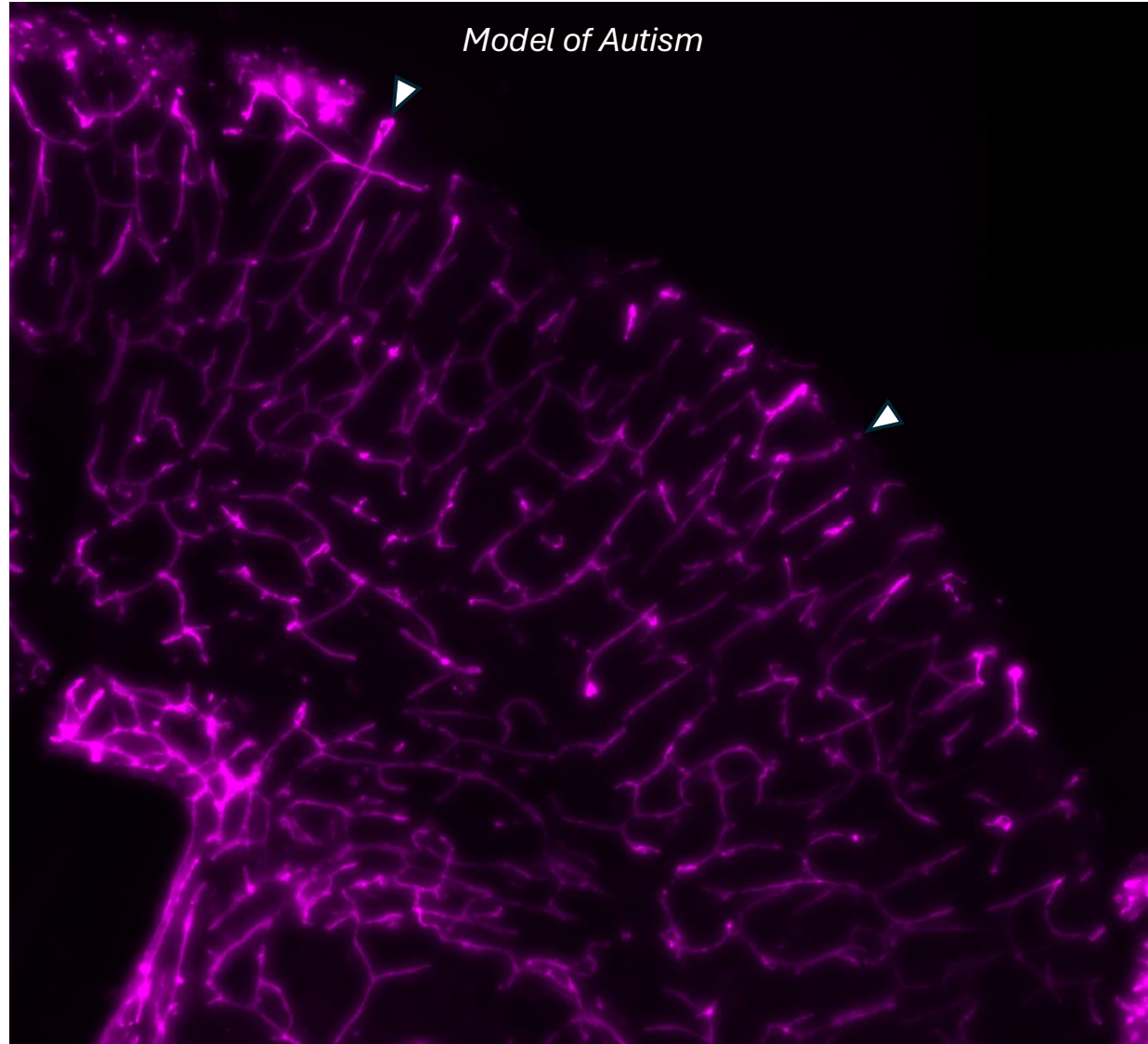
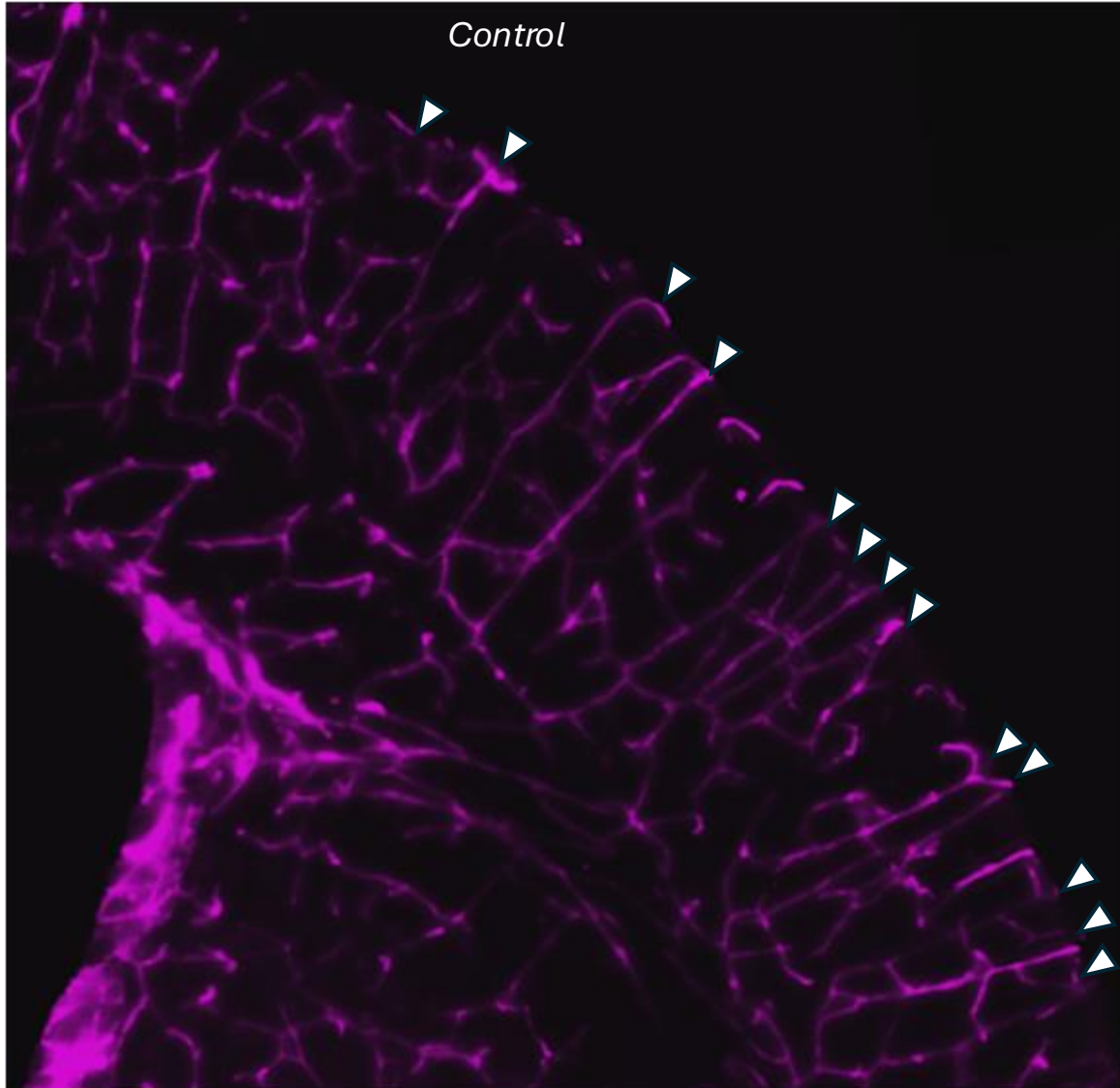
OPCs
Interneurons
Blood vessels

Current Interests

- 1- Neurovascular coupling and its influence in neuronal circuit formation

Current Interests

2- Disruption of neurovascular coupling and its influence in disease



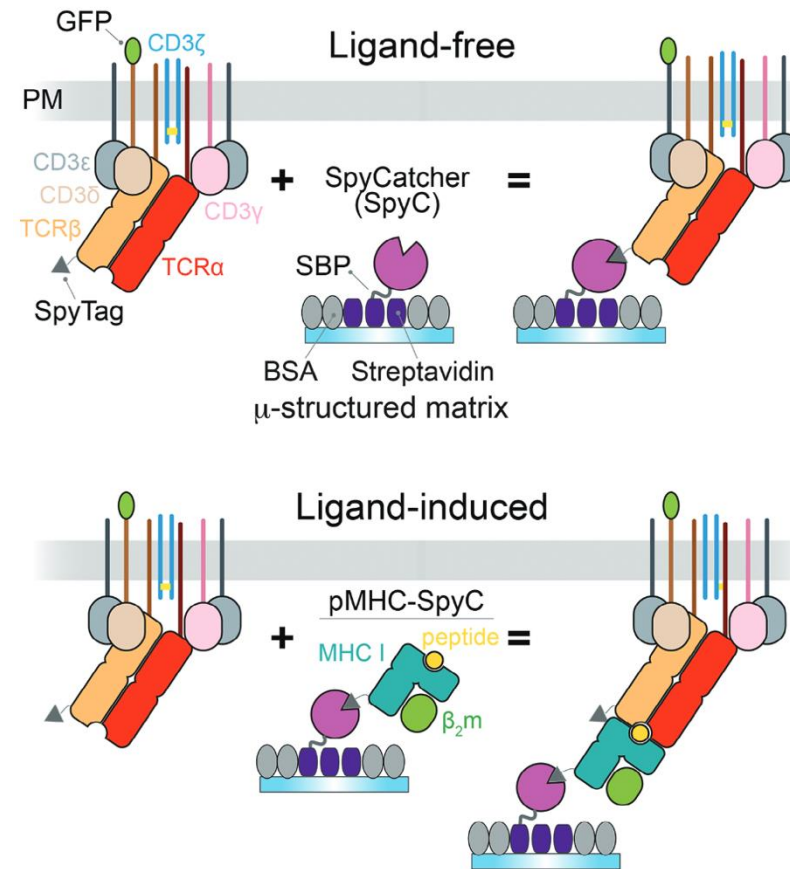
Current Interests

3- How to restore neuronal circuit function *via* blood vessels (cell free therapies)



Maria Florencia
Sanchez

European Institute for
Molecular Imaging,
Munster

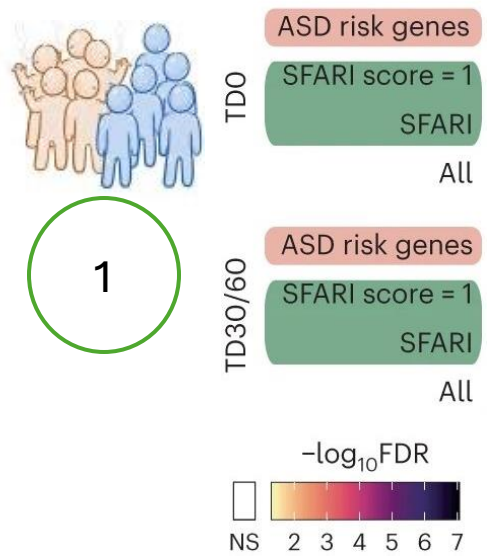


Sanchez *et al.*, Advanced Materials, 2024

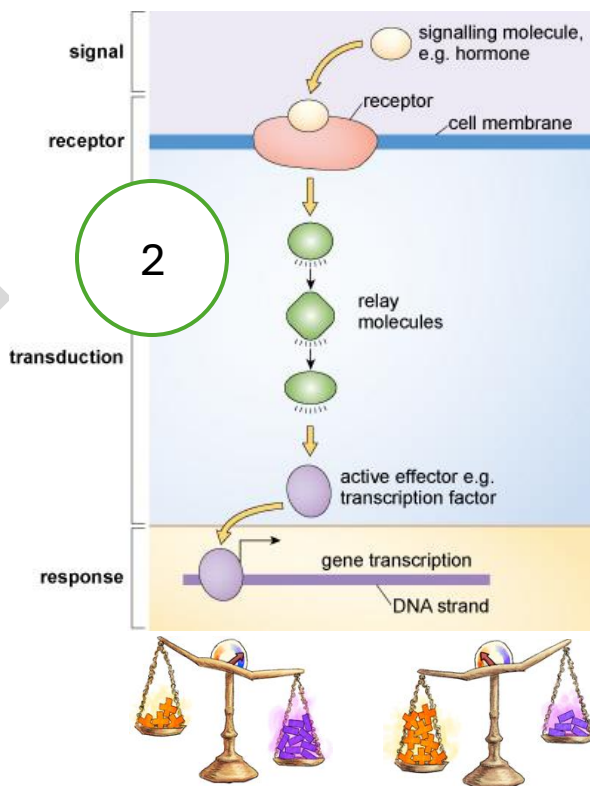
Project Idea



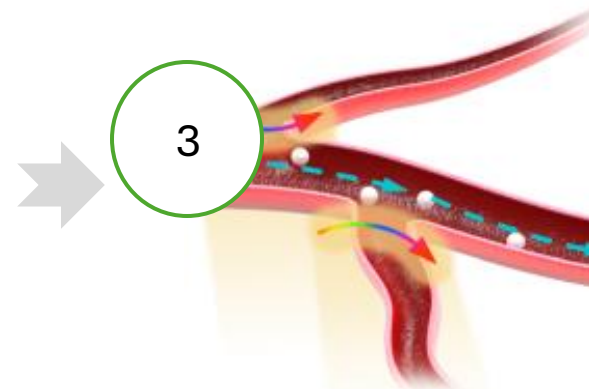
Clinical Information



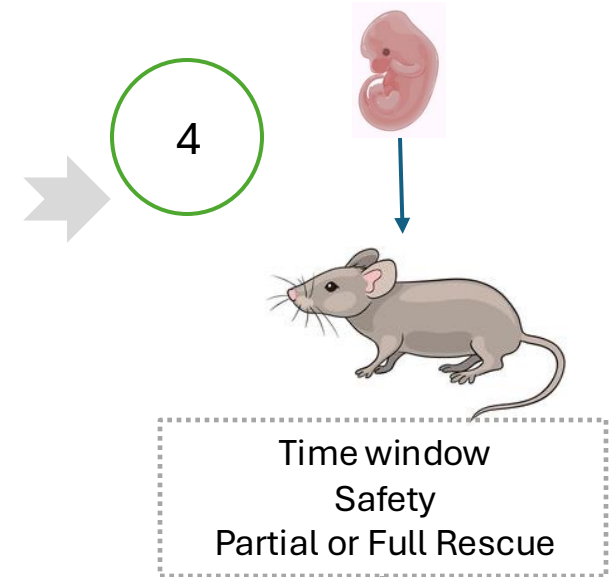
Cellular Pathways



Design of Cell-Free Therapies (Circulation Difusible Particles)



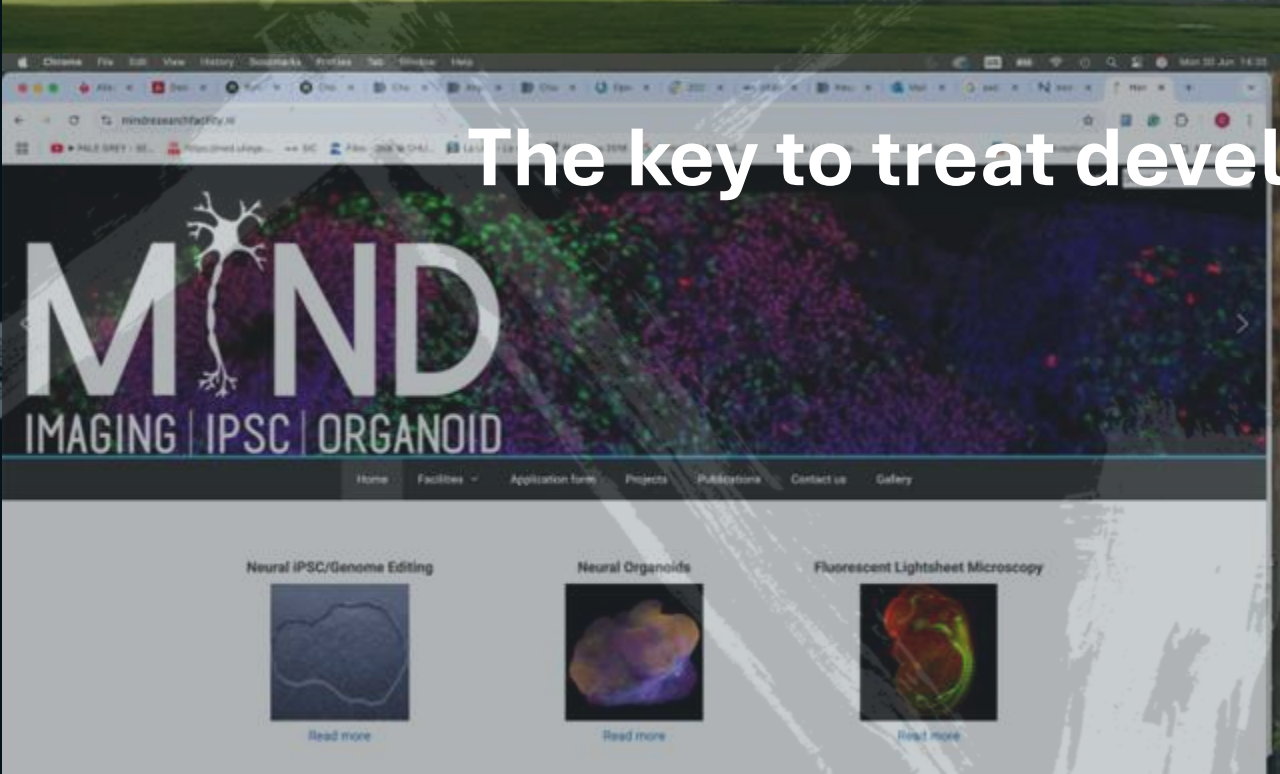
In vivo Assessment



Information Back to the Clinic



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The key to treat developmental brain disorders

