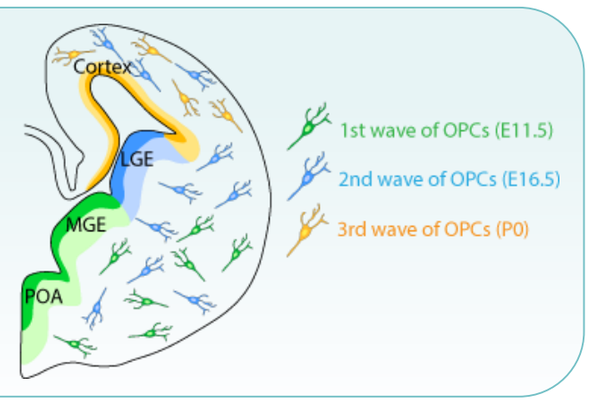
Role of Oligodendrocyte Precursor Cells during Cortical Development

Fanny Lepiemme[1], Carla G. Silva[1*] and Laurent Nguyen[1*]

[1]GIGA-Stem cells / GIGA-Neuroscience, Interdisciplinary Cluster for Applied Genoproteomics (GIGA-R), University of Liège, C.H.U. Sart Tilman, Liège B-4000, Belgium

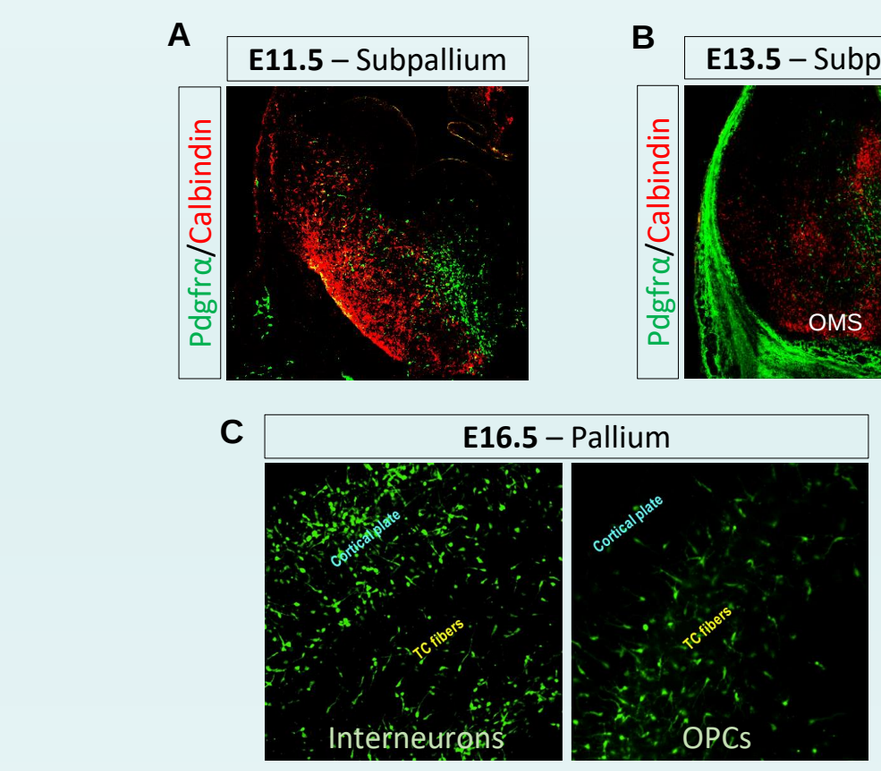
Introduction

The oligodendrocyte precursor cells (OPCs) of the forebrain are derived from distinct progenitor pools. The first cohort is generated at E11.5 in the medial ganglionic eminence (MGE) and the preoptic area (POA) followed by a second cohort born at around E16.5 in the lateral ganglionic eminence (LGE). After birth, OPCs are only generated by pallial progenitors. While the origin of OPCs has been well described, their migration mode and their role during corticogenesis remain poorly understood. In the present study, we combined time-lapse video microscopy and immunostainings to investigate the localization and the migration profile of ventrally-generated OPCs. We also performed *in vitro* analysis to decipher the interaction existing between first-wave OPCs and cortical interneurons, a cell population that migrates concomitantly with OPCs from ventral regions towards the cortex. We further utilized a strategy of cell ablation to unravel the developmental role of embryonically-generated OPCs.



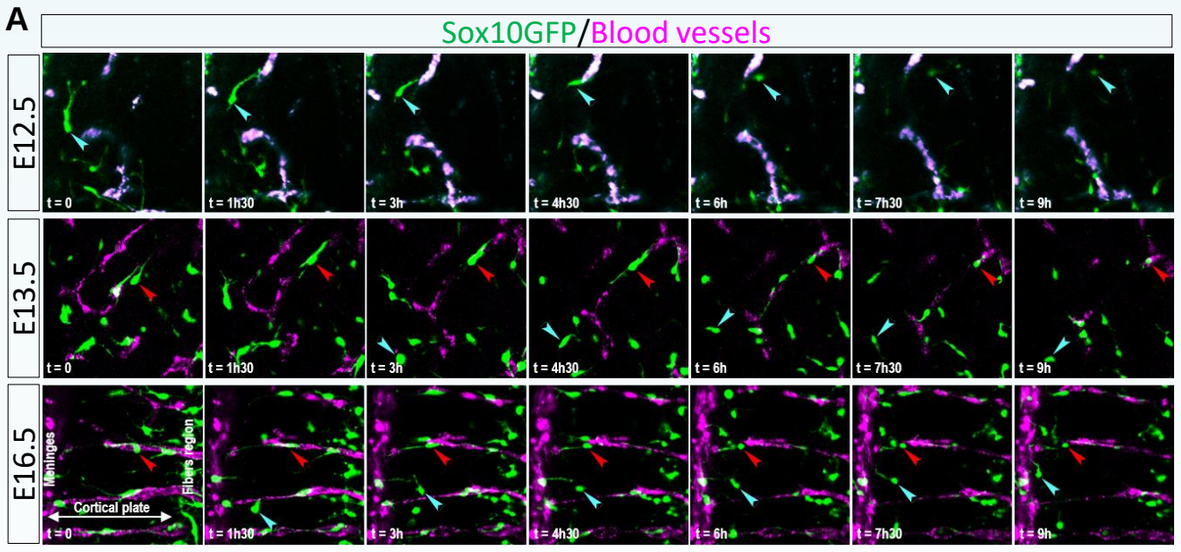
Results

1. Analysis of the Embryonic Distribution of Ventrally-generated OPCs and their Interaction with Interneurons



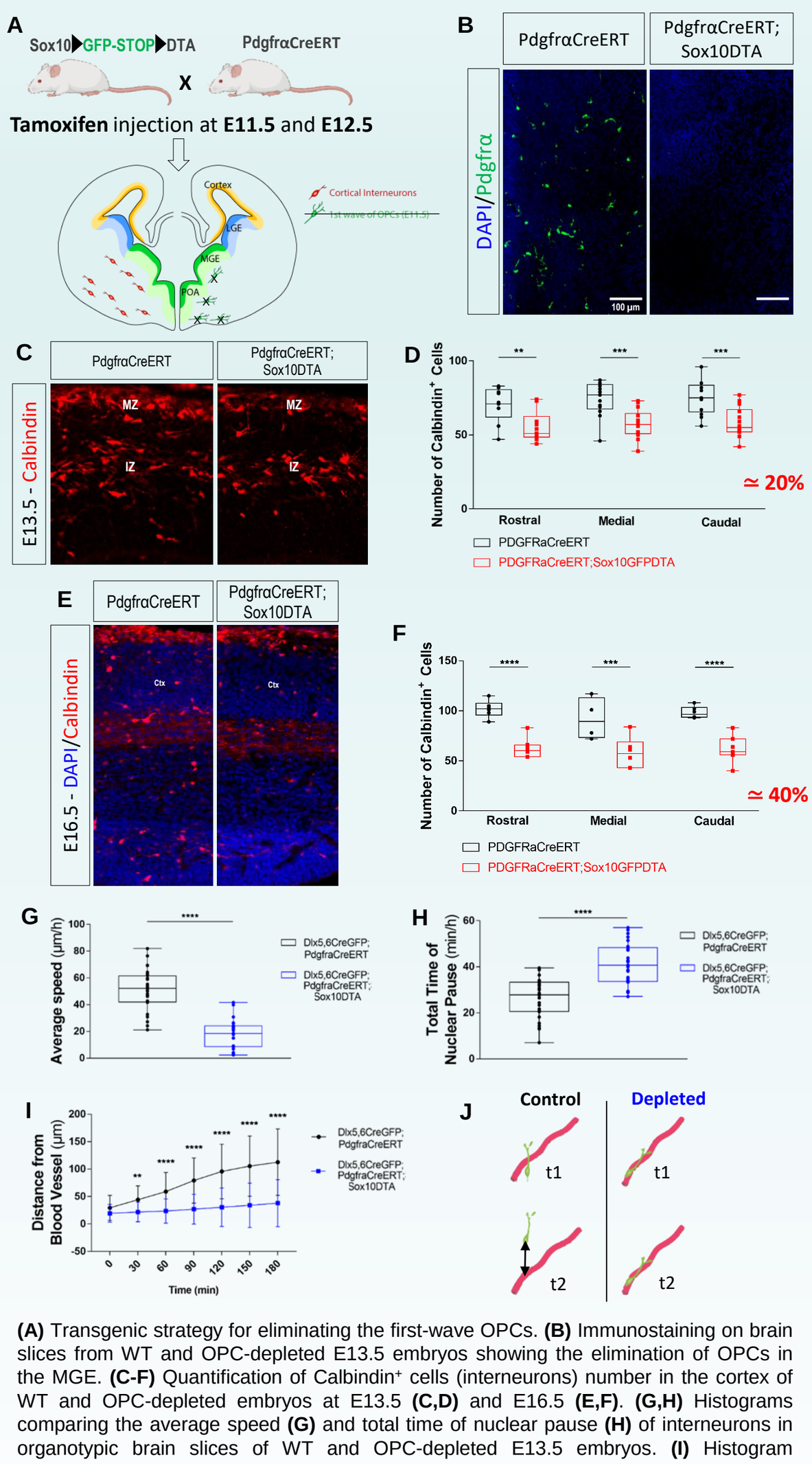
(A-C) Immunostaining showing the distinct distribution patterns of OPCs (Pdgfra+, green) and interneurons (Calbindin+, red) at E11.5 **(A)** and E13.5 **(B)** in subpallial regions, and at E16.5 in pallial regions **(C)**. **(D)** Scheme of the experimental paradigm of co-culture explants from MGE (red) and preoptic area (green). Interneurons (red) and OPCs (green) interact in the space between the two explants. **(E)** Migration behavior of interneurons evaluated by the direction change after an interaction with OPCs. **(F)** Time for a change in behavior of interneurons after a contact with OPCs.

2. Migration Profile and Interactions of OPCs with Blood Vessels in the Pallium



(A) Panels showing interaction of OPCs (green) with blood vessels (stained with IsolectineB4-Cy5, pseudocolor purple) at different embryonic stages. The red arrowheads indicate OPCs migrating along blood vessels and blue arrowheads indicate OPCs migrating without contacting with blood vessels.

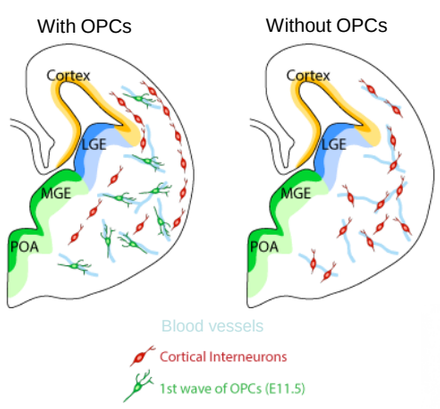
3. Analysis of the Physiological Roles of First-Wave OPCs



(A) Transgenic strategy for eliminating the first-wave OPCs. **(B)** Immunostaining on brain slices from WT and OPC-depleted E13.5 embryos showing the elimination of OPCs in the MGE. **(C-F)** Quantification of Calbindin+ cells (interneurons) number in the cortex of WT and OPC-depleted embryos at E13.5 **(C,D)** and E16.5 **(E,F)**. **(G,H)** Histograms comparing the average speed **(G)** and total time of nuclear pause **(H)** of interneurons in organotypic brain slices of WT and OPC-depleted E13.5 embryos. **(I)** Histogram depicting the relationship between blood vessel and interneuron localization during migration in organotypic brain slices of WT and OPC-depleted E13.5 embryos. **(J)** Scheme representing the behavior of interneurons around blood vessels, during migration.

Conclusion

Our results show that, during embryogenesis, OPCs and interneurons migrate concomitantly but occupy exclusive regions of the forebrain parenchyma likely as a result of a repulsion behavior between these cell populations. First-wave OPC depletion results in a decreased number of interneurons in the cortex at E13.5 and E16.5. This phenotype might be related to the abnormal clustering of interneurons around blood vessels. OPCs migrating on blood vessels might be necessary to repulse interneurons, allowing them to migrate in cortical migratory streams.



Contact: fanny.lepiemme@uliege.be