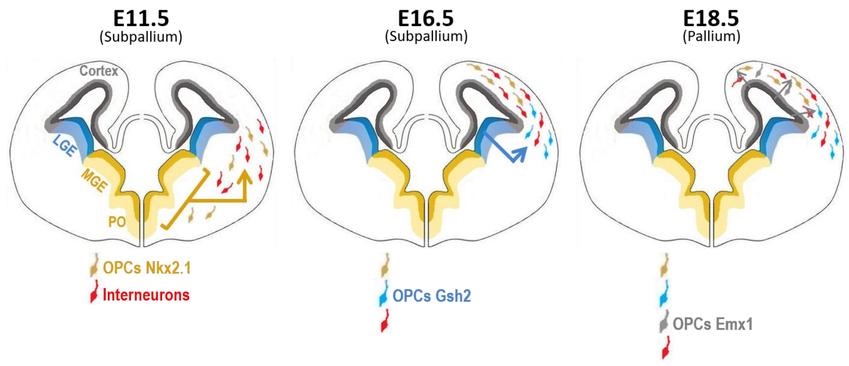
Characterization of Oligodendrocyte Precursor Cell Migration and Function During Corticogenesis

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

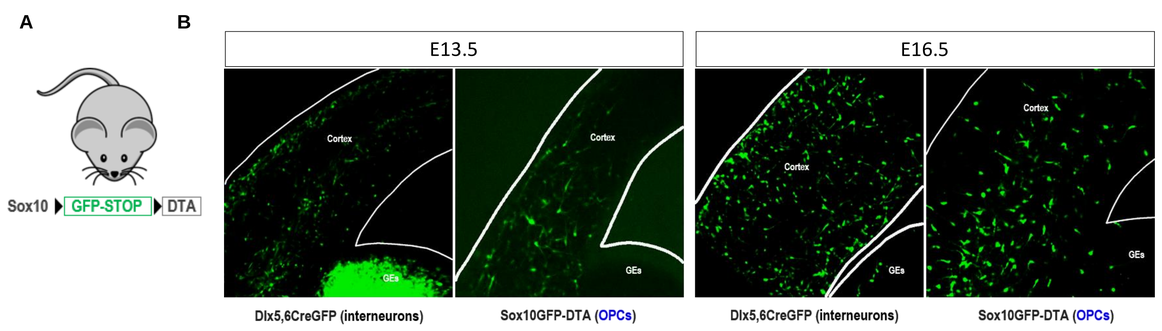
Introduction

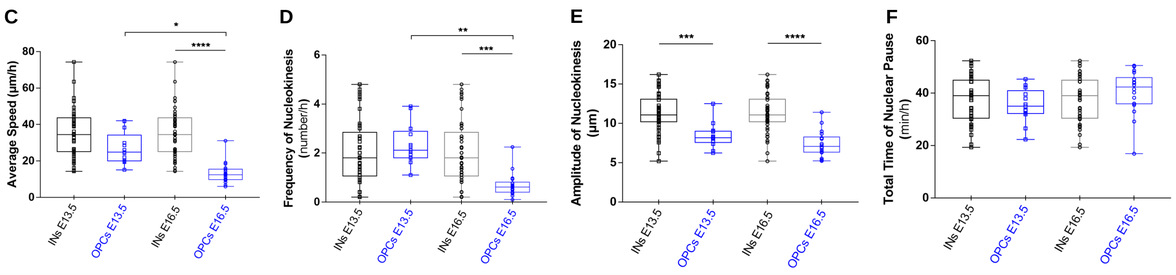
The oligodendrocyte precursor cells (OPCs) are derived from distinct progenitor pools. The two first cohorts are born in the ventral forebrain. The first one is generated at E11.5 in the medial ganglionic eminence (MGE) and the preoptic area (POA) and the second one around E16.5 in the lateral ganglionic eminence (LGE). There is an additional wave of OPCs born at birth in the pallium. While the origin of OPCs has been well described, their migration mode remains poorly understood. In the present study, we performed time-lapse video microscopy to quantify the migration parameters of OPCs at E13.5 and E16.5. We also compared the migration parameters of OPCs generated in the two first generation waves with the migration parameters of cortical interneurons, a cell population that migrates concomitantly with OPCs. We further utilized a strategy of cell ablation to unravel the developmental role of embryonically-generated OPCs.



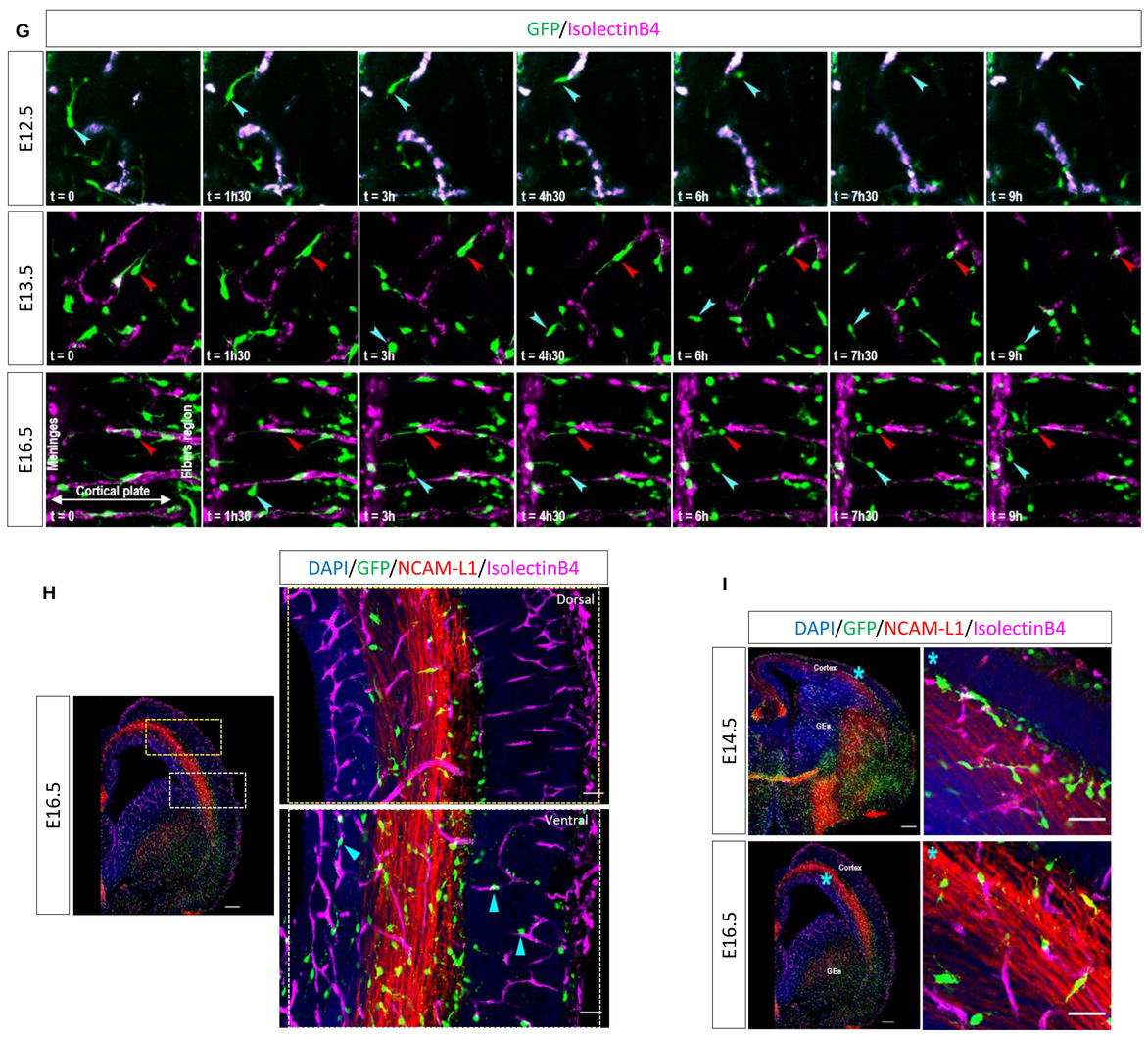
Results

1. Analysis of the Migration Parameters of the First Waves of OPCs



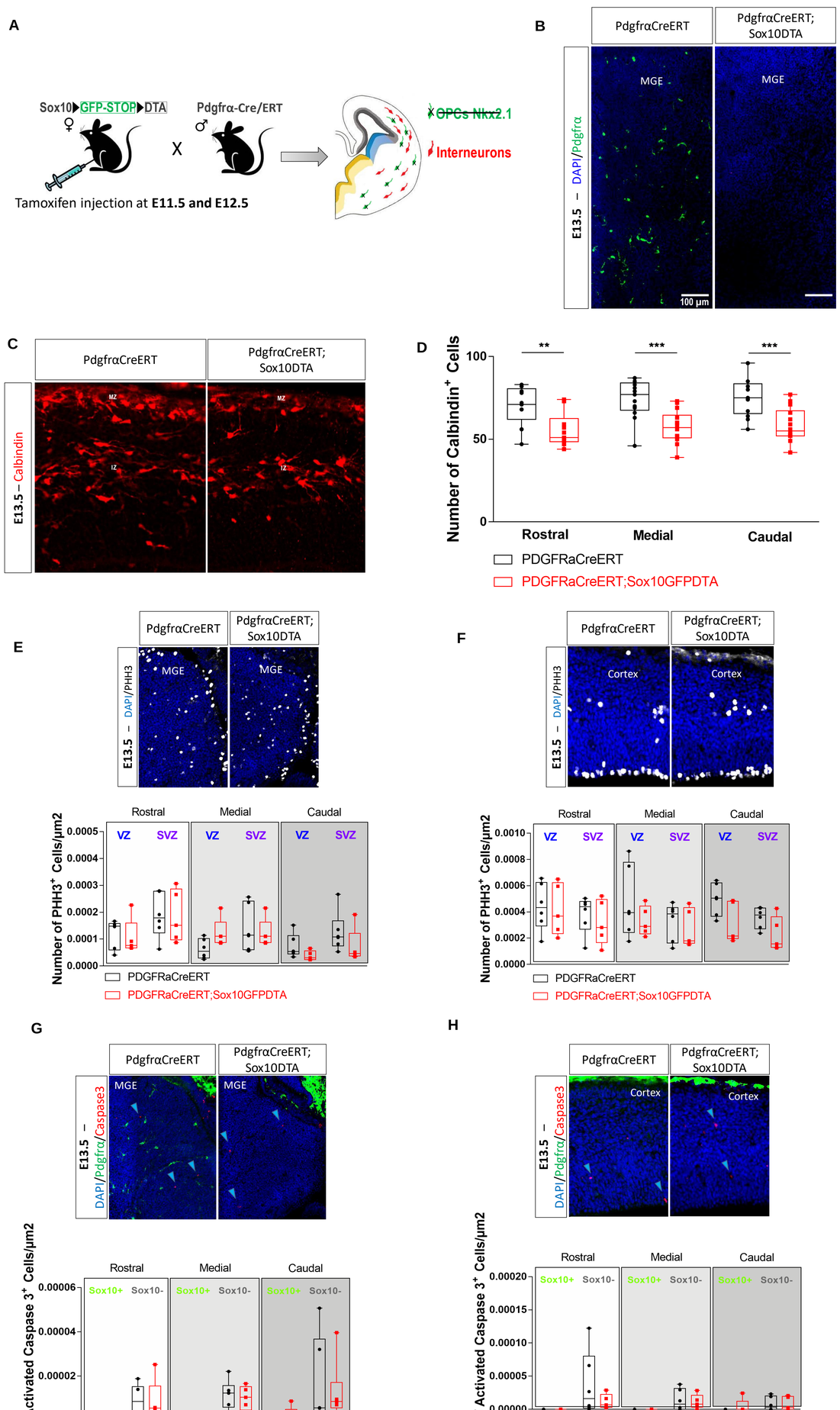


2. Migration Profile and Interactions of OPCs in the Pallium



(A) Transgenic mouse model used in this study (OPCs are identified by the expression of the green fluorescent protein GFP under the control of Sox10 promotor). **(B)** Time-lapse sequence showing the distribution of OPCs (green) in the cortical plate of organotypic brain slices prepared at E13.5 or E16.5. **(C-F)** Histograms comparing the average speed **(C)**, frequency of nucleokinesis **(D)**, amplitude of nucleokinesis **(E)** and total time of nuclear pause **(F)** of OPCs and interneurons at E13.5 and E16.5. **(G)** Panels indicating the 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. **(H)** Immunohistochemistry showing an accumulation of OPCs (green) in brain areas occupied by thalamocortical fibers (staining of NCAM-L1, red). The magnified regions show a gradient of ventro-dorsal invasion of cortical plate by OPCs interacting with blood vessels (purple). **(I)** Immunohistochemistry showing that the interaction of OPCs with thalamocortical fibers is visible at E14.5.

3. Investigation of the Physiological Roles of the First Waves of OPCs



(A) Transgenic strategy for eliminating the first wave of OPCs. **(B)** Immunohistochemistry on brain slices from WT and OPC-depleted E13.5 embryos showing the elimination of OPCs in the MGE. **(C, D)** Quantification of the number of Calbindin$^+$ cells (interneurons) in the cortex of WT and OPC-depleted embryos. **(E, F)** Quantification of proliferation (PHH3$^+$ cells) in the ganglionic eminences **(E)** and cortex **(F)** from WT and OPC-depleted embryos. **(G, H)** Quantification of cell apoptosis (activated Caspase 3$^+$ cells, blue arrowheads) in the ganglionic eminences **(G)** and cortex **(H)** from WT and OPC-depleted embryos.

Conclusions

- **The OPCs and interneurons migrate concomitantly from the subpallium to the cortex with distinct parameters, the OPCs migrating with less discontinuous movements.**
- **The OPCs interact and migrate on various substrates including the thalamocortical fibers and the blood vessels.**
- **The elimination of the first wave of OPCs leads to a reduction of the number of Calbindin$^+$ interneurons invading the cerebral cortex.**

Contact: fanny.lepiemme@uliege.be

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