Deciphering the Mechanisms involved in Interneurons-Oligodendrocyte Precursor Cells Crosstalk in the Developing Cortex – from Mouse to Human

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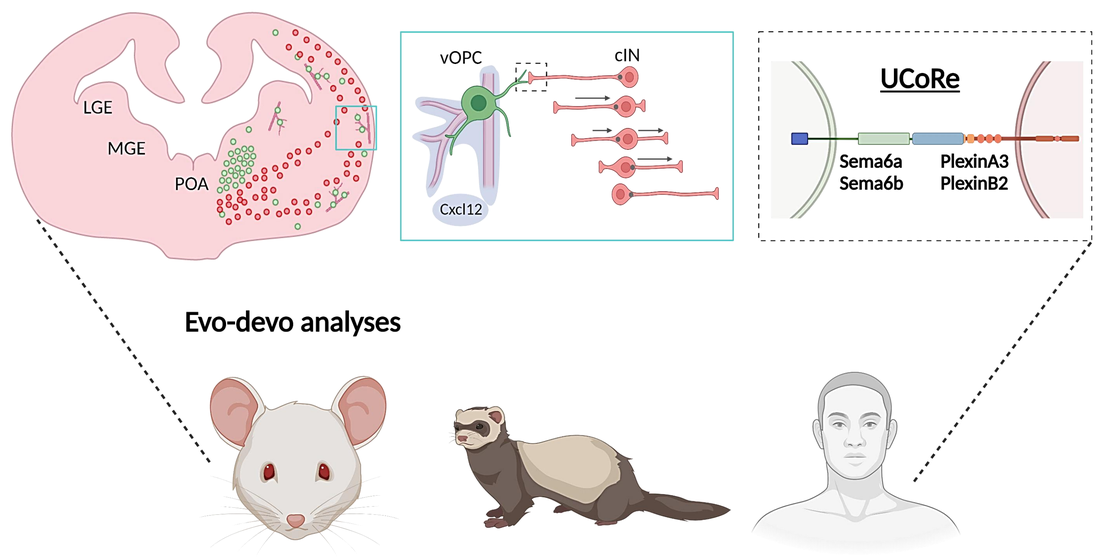
Introduction

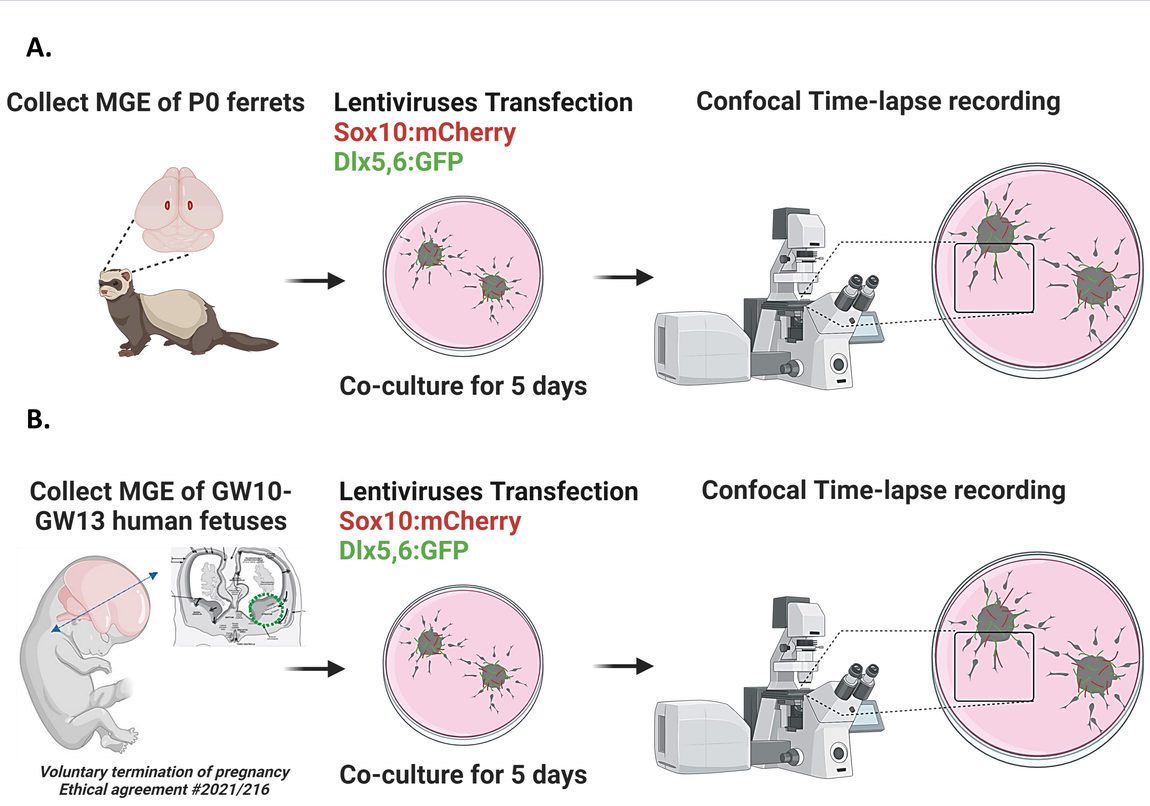
During cerebral corticogenesis, several neural cell types are generated and migrated concomitantly to reach the cortical plate of the presumptive cortex. During their migration, they establish important crosstalk that contribute to their migration, maturation, and network integration. For instance, during early embryogenesis, an interaction between oligodendrocyte precursor cells (OPCs) and interneurons (INs) leads to a unique and unidirectional contact repulsion (UCoRe) of INs without affecting the OPCs. UCoRe redirect INs in their streams of migration into the cortex and prevent their accumulation around blood vessels (BVs). This mechanism was discovered in mice, however; the importance of UCoRe in other mammals was not assessed. Preliminary results, using lentivirus infection on human and ferrets' medial ganglionic eminences (MGE) show a potential conservation of the UCoRe mechanisms in gyrencephalic species. These data suggest a crucial role of the UCoRe for INs and OPCs interactions during brain development among evolution.

Outline



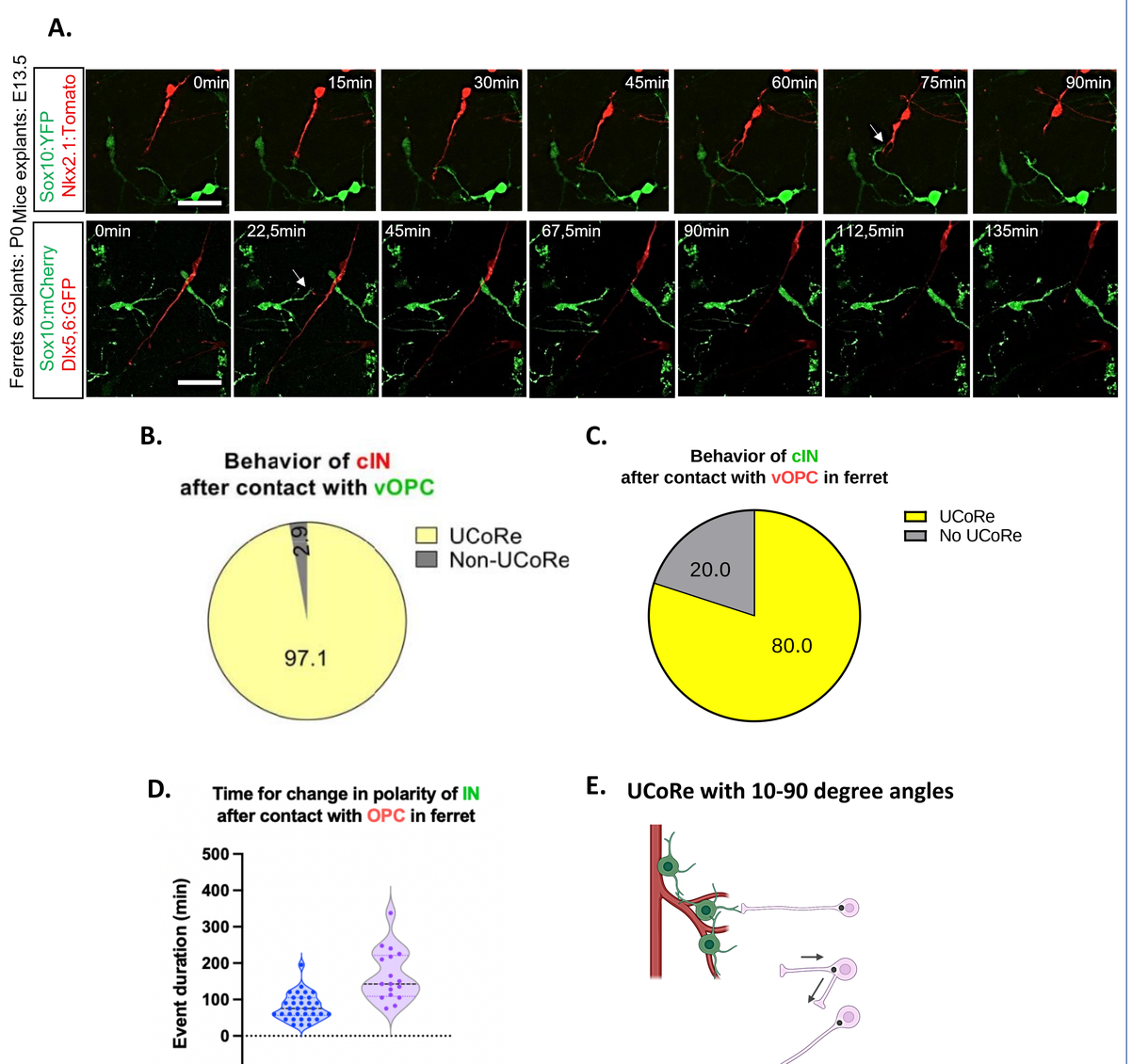
We have designed a project that aim to assess whether UCoRe is conserved in ferrets and humans. By using ventrally-derived OPC and INs, we decipher whether UCoRe occurs in ferret and humans.

Methods



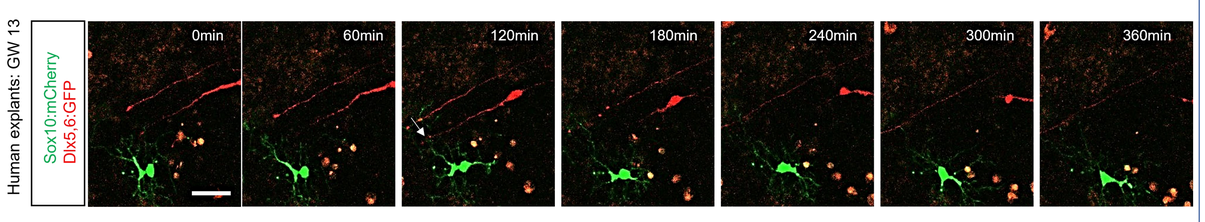
A. To test whether UCoRe is conserved in ferret forebrain, we will perform explant cultures of MGE from newborn ferrets. The explants will be infected prior culture with lentiviruses expressing sox10:mCherry (to label the OPCs) and dlx5,6:GFP (to label the INs) (collaboration with Victor Borell). We will perform time-lapse recording to analyze the interactions between OPCs and INs.
B. To test whether UCoRe is conserved in the human forebrain, we have set up a novel pipeline to collect human fetal brain in the laboratory in collaboration with gynecologists (Prs S. Perrier D'hauterive and A. Firquet, St Rosalie, Hospital, Liege). We have access to fresh human embryos obtained at surgical block after voluntary termination of pregnancy (< 13 gestational week (GW) and 6 days, by Belgian law). MGE explants are dissected and infected with lentiviruses (LV) that labels INs in green and ventrally-generated OPCs in red.

UCoRe interaction in OPC-IN of Ferrets



Preliminary result show that UCoRe is conserved in ferret. **A.** UCoRe has been observed in mice in previous results (Lepiemme et al, 2022). For ferret, contact between interneurons (green; LV of dlx5,6: GFP) and OPC (red; LV of a sox10:mCherry) from a ferret of P0. **B.** The percentage of UCoRe occurrence in mouse. **C.** The percentage of UCoRe occurrence in ferret. A proportion of 80% of Ferrets INs undergo UCoRe. **D.** The violin plot show the timing for changing polarity after UCoRe in mice and ferrets. **E.** The polarity reversal in Ferret after UCoRe show a different angle compared to mice UCoRe.

UCoRe interaction in OPC-IN of Human



Our preliminary experiments of human tissues show that both cell types can be lived imaged. The INs touch OPCs twice and retract back to migrate to an opposite direction. These data reveal a possible evolutionary conservation of UCoRe in the human forebrain. However, more experiments will be needed to confirm the characteristics of UCoRe and its downstream intracellular pathways in human resemble those observed in mice.

Conclusion

In conclusion, some differences were observed between mice, ferrets, and human. The average time of polarity change of INs after contact is longer in ferret (110.12min) than in mice (78.6min). These results suggested that UCoRe is conserved but protracted in time in ferret. For the preliminary human study, we can see that UCoRe can be observed in human tissue. We will keep collecting human tissue and further analyze the difference between species to confirm our findings.

Reference

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