Role of *Egfr* in Forebrain Development

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INTRODUCTION

The mammalian brain is arguably the most complex of all biological systems. The cerebral cortex lies at the highest level of information processing within the mammalian brain but its development consists of two important transitions; one from neuroepithelial expansion to neurogenesis during early cortical development and another during perinatal periods when neurogenesis switches to gliogenesis in a subset of cortical progenitors. The mechanisms that control these two transitions are important to understanding a wide range of central nervous system (CNS) disorders including neurodevelopmental disorders.

We have identified the Epidermal Growth Factor Receptor (Egfr) as a potent regulator of a unique set of gliogenic progenitors during the neurogenesis to gliogenesis switch in the cortex. Using a rigorous genetic approach we have discovered that these unique Egfr-dependent gliogenic progenitors form a gradient along the rostro-caudal extent of the cortex.

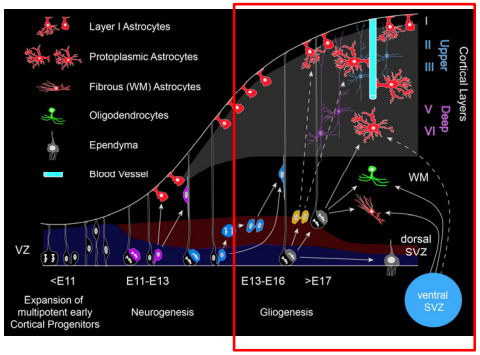

Fig 1. Time graph for formation of glial cells. The first transition will produce neurons followed by a later transition which generates all the glial in the cortex.

STUDY DESIGN

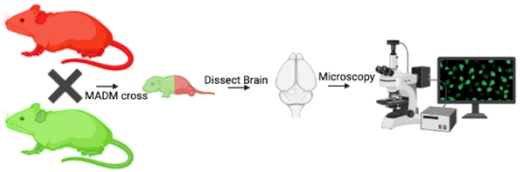

Fig 2. Schematic of the overall experimental process. Mice are crossed to generate tissue specific activation of reporter genes. Brains are dissected from young mice and sectioned by a vibratome. The sections are fixed and analyzed with confocal microscopy.

RESULTS

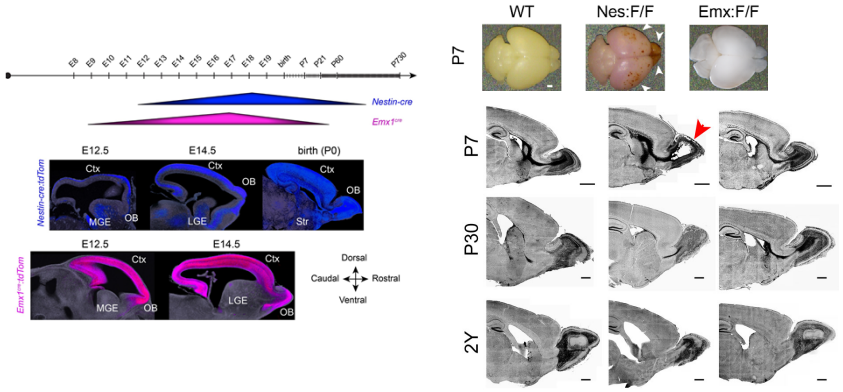

Fig 3. Conditional deletion of *Egfr* in the CNS using Nestin-cre (*Nes:F/F*) and Emx1-cre (*Emx:F/F*) lines of mice.

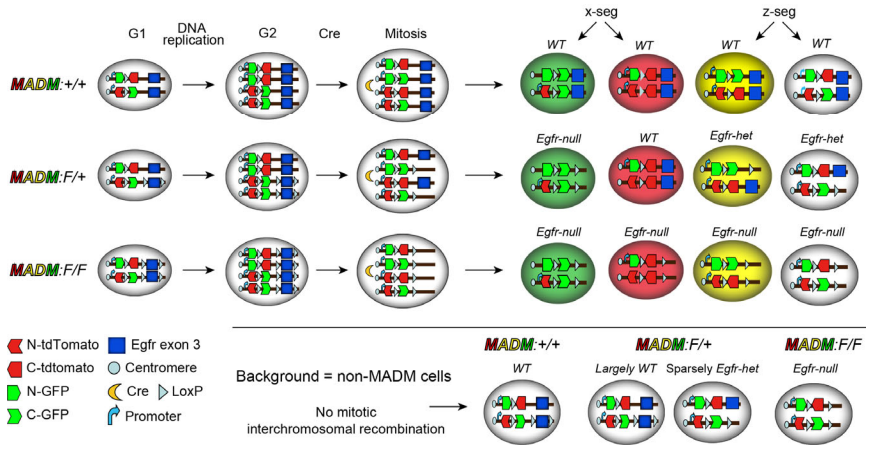

Fig 4. *Egfr* gene dosage model using Mosaic Analysis with Double Markers (MADM)

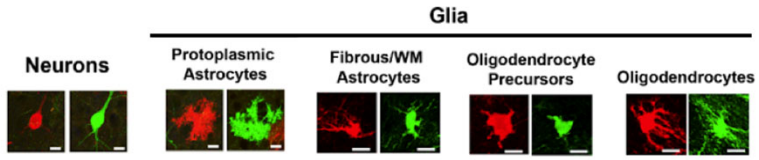

Fig 5. Phenotypes for different neuron and glial cells

RESULTS

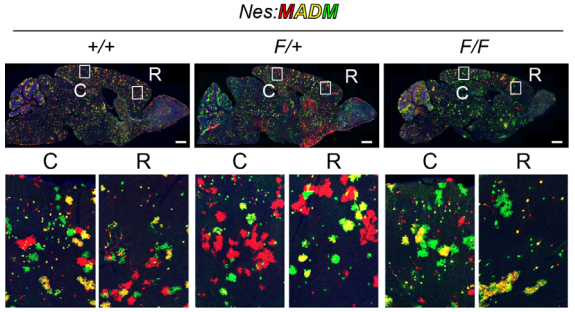

Fig 6. Analysis of *Nes:MADM* cortices with various Egfr genotypes reveals dosage responses in glial lineages

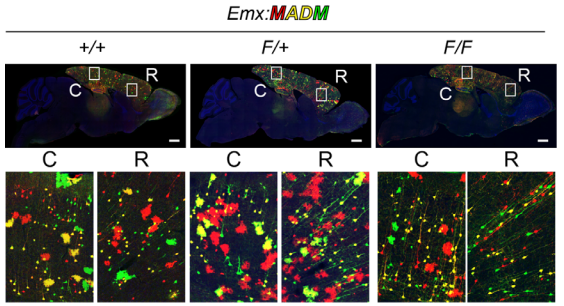

Fig 7. Analysis of *Emx:MADM* cortices with various Egfr genotypes confirms dosage responses in glial lineage, and further reveals region-specific gliogenesis that is Egfr-dependent

CONCLUSION

- Discovery of a region-specific and Egfr-dependent gliogenic population in the cortex.
- It appears that a ventral and caudally situated population of Egfr-independent gliogenic progenitors compensate for loss of Egfr-dependent glia.

FUTURE WORK

- Describe the identity of Egfr-dependent and Egfr-independent gliogenic progenitors using transcriptomic and single cell RNA-seq approaches
- Test the requirement for identified factors in region-specific gliogenesis in the cortex

REFERENCES

1. Johnson, C.A., and Ghashghaei, H.T. *Development* 147.4 (2020).
2. Aguirre, A., Rubio, M. E., & Gallo, V. (2010). *Nature*, *467*(7313), 323-327.