Evolution of cortical progenitor cells: much to gain, much to loose

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The evolutionary expansion and folding of the mammalian cerebral cortex resulted from amplification of progenitor cells during embryonic development, but the cellular and genetic mechanisms behind this key process remain poorly understood. Here I will discuss our latest results on this fascinating question, first showing the increased complexity of progenitor cell types in ferret and human compared to mouse. Our ferret scRNAseq data from specific germinal layers and developmental stages reveals an unprecedented heterogeneity of progenitor cell subtypes that are related by parallel cellular lineages, including different self-amplificative activity, which converge on an otherwise common neurogenic path. Intriguingly, the amplification of cortical progenitor cells during mammalian evolution was reversed in the rodent lineage after splitting from primates, leading to smaller and smooth brains. Genetic mechanisms underlying this secondary loss in rodent evolution remain unknown. In the second part of my presentation, I will discuss our most recent results identifying for the first time a gene (*miR-3607*) selected for secondary loss during mammalian evolution to limit progenitor cell amplification and, potentially, cortex size in rodents. This microRNA is expressed embryonically in the large cortex of primates and ferret, distant from the primate-rodent lineage, but not in mouse. Experimental expression of *miR-3607* in embryonic mouse cortex led to increased Wnt/β–Catenin signaling, amplification of Radial Glia Cells (RGCs) and expansion of the Ventricular Zone (VZ), via blocking the β–Catenin inhibitor APC. In summary, I will illustrate how the evolution of the mammalian neocortex involved both the gain and loss of cellular and molecular players.

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