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Abstract SENC 2021 – 300 words max

Title: Delving into the generation of cortical astrocyte diversity and plasticity using multicolor lineage tracing tools

Topic: Developmental Neurobiology

Abstract:

Mammalian cerebral cortex functions rely on the cooperation of distinct cell types including neurons and glial cells that must be produced in defined proportions and whose imbalance can lead to severe neurodevelopmental disorders. During cerebral cortex development, neurons and glial cells, including astrocytes, are produced sequentially by neural progenitors and ensure together proper synaptic functions. While neurons have been extensively studied in the context of physiological and pathological development, cellular and molecular players responsible for the emergence of cortical diversity, and in particular astrocyte generation, remain poorly described. Astrocytes constitute an heterogeneous population in terms of morphology, molecular marker expression and function, within and among brain regions in mammals. Using combinatorial genetic markers and multicolor imaging techniques, we marked adjacent cortical progenitors with rare color markers prior to gliogenesis and tracked their descent over long periods of time to study astrocyte development. We showed that cortical astrocyte clones display extensive variability in terms of structural organization, location, number and subtype of generated cells. Furthermore, we demonstrated that cortical astrocyte network is generated through two developmental stages that comprise a dynamic phase of proliferation and spatial dispersion followed by a maturation phase where morphology complexity and volume increase at the single cell level. In addition, we determined that astrocyte network is supplied both pre- and perinatally by cortical progenitors. Altogether, our results highlighted the plasticity of astrocytes that probably acquire their subtype features through interactions with their environment. To better understand the emergence of cortical astrocyte diversity, we are now studying in more detail the embryonic origin of astrocytes during brain development. Our work will allow to better understand cortical astrogliogenesis and its critical cellular and molecular components that could be altered in neurodevelopmental pathologies.