TITLE: “Coming from within: cell intrinsic modulators of quiescent neural stem cells”

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ABSTRACT: Tissue homeostasis and repair in a variety of mammalian organs relies on the persistence of somatic stem cell reservoirs. Throughout adulthood, these resident stem cells remain predominantly in a reversible resting state known as quiescence. Within the brain, a prominent quiescent neural stem cell (NSC) reservoir is maintained in the subgranular zone of the hippocampal dentate gyrus. The development of this stem cell niche ends during the postnatal period, coinciding with the transition of NSCs from the proliferative state into the definitive quiescent state. Thereafter, only a minor fraction of the adult hippocampal radial glia-like NSCs becomes active and engages in a neurogenic cascade that leads to the production of new functional granule neurons involved in learning and memory tasks. Recent studies suggest that quiescence is more than just a passive latency condition developed to protect NSCs from the drawbacks of hyperproliferation. Despite being metabolically less active than their proliferating counterparts, quiescent NSCs are held in a flexible and highly dynamic state that allows them to respond to changes in their microenvironment. This state requires a tight and complex regulation of gene expression. We previously reported that the equilibrium between NSC quiescence and NSC activation leading to productive neurogenesis depends on the interplay of a variety of local extrinsic niche signals, the BMP and Wnt family being of utmost importance. We now provide evidence for the fine-tuning of BMP and Wnt signalling by cell intrinsic post-transcriptional mechanisms, including mRNA splicing, microRNA-mediated events and proteostasis.