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Post-translational regulation of stem cell quiescence and activity in the adult brain

Neural stem cells located in restricted regions of the adult brain produce neurons that have important functions in memory and mood control. While the niche signals that control neural stem cell fates have been extensively investigated, little is known of the intrinsic mechanisms that mediate the activity of these extrinsic signals and implement appropriate fate decisions. Using high throughput genomic analysis and genetic approaches in stem cell cultures and in vivo, we characterise transcription factors that regulate the transitions between neural stem cell quiescence, activation and differentiation in response to niche signals.

We found that expression of the transcription factor *Ascl1* by stem cells of the adult hippocampus is essential for their activation, and that regulation of *Ascl1* protein levels determines the rates at which stem cells self-renew and new neurons are produced. Reduced levels of *Ascl1* slow down stem cell proliferation and neurogenesis while increased levels accelerate proliferation and lead eventually to stem cell exhaustion and inhibition of neurogenesis. *Ascl1* protein levels are controlled by different post-translational mechanisms in proliferating stem cells and quiescent stem cells.

Interestingly, we have obtained evidence that stem cells that have proliferated and returned to quiescence are molecularly and functionally distinct from stem cells that have never be active.