## The role of lipid droplets for neural stem/progenitor cells

The brain is formed during embryonic development, where neural stem/progenitor cells (NSPCs) divide and generate neurons, glial cells as well as new NSPCs. Few NSPCs persist throughout adulthood, allowing the generation of new neurons in a process called adult neurogenesis, in defined brain regions: in the subventricular zone of the lateral ventricles in mice and in the hippocampus of both mice and humans. Lipid metabolism has been shown to be important for adult neurogenesis. In fact, NSPCs rely on fatty acid oxidation and *de novo* lipogenesis for proper maintenance and proliferation. Lipid droplets (LDs) are found at the crossroad of these two key metabolic processes, allowing the storage of lipids for later usage. In addition to their main lipid core, these organelles are also coated by specific proteins known as LD coat proteins, which contribute to both storage and usage of lipids.

In this thesis, we show that LDs are abundant in NSPCs *in vitro*. We also show that LDs influence NSPC proliferation and metabolism. More precisely, we found that NSPCs can contains variable amounts of LDs, which can be inherited asymmetrically upon division, leading to differences in proliferation and the metabolic capacity. Moreover, we observed that manipulating LDs either by inhibiting their build-up or breakdown by targeting the key adipose triacylglyceride lipase (ATGL) led to impaired proliferation as well. We also found that upon differentiation into neurons or astrocytes *in vitro*, LDs change in number and size. To follow-up on these findings, we generated a triple mutant mouse model where ATGL can be genetically removed (ATGL KO). Preliminary results indicate that ATGL KO leads to defects in proliferation in hippocampal NSPCs *in vivo*. Moreover, we could determine other LD coat proteins in NSPCs. In this list of proteins, some were known to be associated with cell cycle regulation. Using a cell cycle reporter system, we found abundant nuclear LDs and that LDs vary in number and volume along the cell cycle. By manipulating cytoplasmic and nuclear LDs through lipid loading, we could disturb cell cycle transition and block the cells at the S-phase entry. Taken together, our results suggest that in NSPCs, lipid metabolism, proliferation and cell cycle progression are somehow linked, with LDs playing a crucial part in this link. However, the exact underlying mechanisms remain to be determined.