ASTROCYTES AND ADULT NEURAL PROGENITORS CROSS-TALK: RELEVANT ROLE OF NF-kB p50

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In previous work we demonstrated that NF-κB p50 acts as regulator of adult hippocampal neural progenitor cells (ahNPC) (Denis-Donini, 2008). Indeed, p50KO mice are characterized by remarkably reduced hippocampal neurogenesis and a selective defect in hippocampal-dependent short-term memory. More recently we observed that when cultured in vitro, ahNPC from WT and p50KO mice are not significantly different in their neurogenic potential. This observation prompted us to investigate cell autonomous and non cell-autonomous consequences of p50 absence on neuronal fate specification of ahNPC. We focused our attention on astrocytes, known to provide soluble pro-neurogenic signals (Song, 2002), and investigated the influence of WT and p50KO astrocyte conditioned media (ACM) on WT and p50KO ahNPC differentiation. Interestingly, while WT ACM promoted both neuronal and astroglial differentiation, p50KO ACM only supported astroglial differentiation of WT ahNPC. By using a LC-MS/MS approach we identified proteins which are differentially secreted by p50KO compared to WT astrocytes. Among them, lipocalin-2 (LCN-2) was recognized as a novel astroglial-derived signal regulating neuronal fate specification of ahNPC. In addition to that, we demonstrated p50KO NPC unresponsiveness to both neuronal and astroglial fate specification signals derived from both WT and p50KO ACM. Finally, we identified reduced expression of α2δ1, a thrombospondin-1 receptor, as another phenotypic change occurring in ahNPC in absence of p50. Our findings suggest that neurogenic defects observed in vivo in p50KO mice may rely on both cell autonomous and non cell autonomous defects of NPC (Cvijetic, 2017). Moreover these results further increase our current knowledge on the relevance of astrocyte-NPC communication in the modulation of adult hippocampal neurogenesis.

Denis-Donini et al. (2008). J Neurosci. 28, 3911-9.

Song et al. (2002). Nature. 417, 39-44.

Cvijetic et al. (2017). Glia. 65, 169-81.