ORAL COMMUNICATIONS

INVESTIGATING THE ROLE OF NR2F1 IN NEURAL STEM CELL QUIESCENCE AND ACTIVATION IN THE ADULT SUBVENTRICULAR ZONE

Iacono F.[1], Licursi V.[2], Quaresima S.[1], Manzini V.[2], Felli A.[1], Lippolis A.[3|4], Miranda Banos M.E.[1], Cacci E.[1], Peretto P.[3|4], Studer M.[5], De Marchis S.[3|4], Lupo G.[1], Bonzano S.[3|4]

[1]Department of Biology e Biotechnologies Charles Darwin, Sapienza University of Rome, Italy; [2]Institute of Molecular Biology and Pathology (IBPM), National Research Council (CNR), Rome, Italy; [3]Department of Life Sciences and Systems Biology (DBIOS), University of Turin, Italy; [4]Neuroscience Institute Cavalieri Ottolenghi (NICO), Regione Gonzole 10, Orbassano (TO), Italy; [5]Univ. Côte d'Azur (UniCA), CNRS, Inserm, Institut de Biologie Valrose (iBV), Nice, France

Adult neurogenesis in mice occurs in specialized brain niches, including the subventricular zone (SVZ) of the lateral ventricles and the subgranular zone (SGZ) of the dentate gyrus, where neural stem cells (NSCs) balance quiescence and activation towards proliferation and differentiation in response to various stimuli. This balance is essential to preserve the NSC pool, ensuring lifelong neurogenesis and brain plasticity. Although quiescent and activated NSCs show key transcriptomic differences, the underlying transcriptional regulators remain unclear.

The transcription factor NR2F1 controls neural progenitor proliferation and differentiation in mouse embryos. NR2F1 is also expressed in adult NSCs, but its role in their quiescence and activation is not known. Using in vitro culture models of quiescent and activated SGZ and SVZ NSCs, we found consistent upregulation of NR2F1 in quiescent NSCs at the mRNA and protein levels, suggesting that NR2F1 promotes NSC quiescence. Supporting this hypothesis, conditional NR2F1 deletion in vivo increases NSC proliferation in the adult SVZ, suggesting that NR2F1 deficiency enhances NSC activation. By means of CUT&RUN analysis, we have identified the genomic targets of NR2F1 in SVZ NSCs, which include the promoters of genes involved in NSC self-renewal, mitochondrial function, and purine metabolism. Furthermore, we have generated SVZ NSC lines lacking NR2F1 function, and we are using them to address the functional role of NR2F1 in the regulation of NSC cell cycle and the transcriptomic pathways mediating this role.

Acknowledgments: This work was supported by PRIN 2022 (2022WJFN5X).