Non-coding RNAs and in particular microRNAs tune brain cell differentiation and synaptic development, and modulate brain functions such as synaptic plasticity, memory formation and behavioral performances. Our research, aims to identify long noncoding RNAs (lncRNAs) and/or microRNAs as well as their interactions, and to investigate their roles in neuronal and glia cells during physiological and pathological conditions. Main focus is the study of these molecules in Ageing and Alzheimer’s Disease (AD).

Primary rodent neural cell cultures, cell lines, human neuronal and glia cells differentiated from iPSC (induced pluripotent stem cells)-derived NSC (neural stem cells) as well as mouse models are instrumental to our studies.

Previous findings in our laboratory have shown that miR-101 regulates directly AD-related genes, Amyloid precursor protein (APP) and Ranbp9, in rodent hippocampal neurons in vitro and in vivo (Vilardo et al., 2010; Barbato et al., 2014). More recently we found that inhibition of miR-101 post-transcriptional regulation in CA1 hippocampal neurons of adult C57BL/SJ mice, by stereotaxic injection of a lentiviral miRNA sponge, leads to cognitive decline (Barbato et al., 2020). The cognitive impairment features were associated with increased hippocampal expression of relevant miR-101 target genes, APP, RanBP9 and Rab5 and overproduction of amyloid beta (Aβ) 42 levels, the more toxic species of Aβ peptide. Notably, phosphorylation-dependent AMP-activated protein kinase (AMPK) hyperactivation is associated with AD pathology and age-dependent memory decline, and we found AMPK hyperphosphorylation in the hippocampus of pLSyn-miR-101 sponge mice. Further characterization of the molecular pathways involved in hippocampal dependent cognitive decline after miR-101 downregulation are ongoing. We are also planning to search for functional effects of miR-101 inhibition in neurons on glia cells using co-culture models.

Finally, we are also searching for lncRNAs that might regulate miR-101 and/or other microRNAs and pathways associated to Ageing/AD by bioinformatics and wet studies.

References:


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