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P39. THE MICRO RNA-29A MODULATES 5-HTR7 EXPRESSION AND ITS MORPHOGENIC EFFECTS IN HIPPOCAMPAL NEURONS

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miRNAs are master regulators of gene expression in diverse biological processes, including neuronal differentiation, dendritic arborization, synaptic plasticity, neuronal survival and regeneration. The identification of their physiological target genes remains one of the outstanding challenges. Recently, we demonstrated that the activation of serotonin receptor 7 (5-HT7R) plays a key role in regulating the neuronal cytoarchitecture, synaptogenesis and synaptic plasticity during embryonic and early postnatal development of the CNS. However, the possible interplay between miRNAs and 5-HT7R has not yet been studied. Starting from a computational prediction of microRNAs in 5-HT7R mouse gene, we identify miR-29-3p as an important regulator of 5-HT7R gene expression. Using a luciferase reporter system we demonstrate that miR-29a binds to 3'UTR of 5-HT7R mRNA and concomitantly downregulates its expression. On the contrary. the expression of other serotonin receptors, such as 5-HT1AR and 5-HT6R, is not affected by miR-29a. Using primary neuronal cultures from the postnatal hippocampus we show that over-expression of miR-29a impairs neurite outgrowth induced by 5-HT7R stimulation, as well as downstream signalling transduction pathways. In addition, we observed that the upregulation of miR-29a in the late postnatal stages (P20) of hippocampal development parallels with the downregulation of 5-HT7R. Our data support the idea that this miRNA could be a physiological modulator of 5-HT7R, involved in shaping hippocampal neural circuits during development. Understanding the way miR29a is contributing to the regulation of 5-HT7R-dependent structural plasticity in the CNS may provide clues to establish novel therapeutic strategies for neurodevelopmental diseases associated with altered brain connectivity.