Cholinesterase-Targeting microRNAs Identified in silico Affect Specific Biological Processes

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Abstract:

MicroRNAs (miRs) have emerged as important gene silencers affecting many target mRNAs. Here, we report the identification of 244 miRs that target the 3'-untranslated regions of different cholinesterase transcripts: 116 for butyrylcholinesterase (BChE), 47 for the synaptic acetylcholinesterase (AChE-S) splice variant, and 81 for the normally rare splice variant AChE-R. Of these, 11 and 6 miRs target both AChE-S and AChE-R, and AChE-R and BChE transcripts, respectively. BChE and AChE-S showed no overlapping miRs, attesting to their distinct modes of miR regulation. Generally, miRs can suppress a number of targets; thereby controlling an entire battery of functions. To evaluate the importance of the cholinesterase-targeted miRs in other specific biological processes we searched for their other experimentally validated target transcripts and analyzed the gene ontology enriched biological processes these transcripts are involved in. Interestingly, a number of the resulting categories are also related to cholinesterases. They include, for BChE, response to glucocorticoid stimulus, and for AChE, response to wounding and two child terms of neuron development: regulation of axonogenesis and regulation of dendrite morphogenesis. Importantly, all of the AChE-targeting miRs found to be related to these selected processes were directed against the normally rare AChE-R splice variant, with three of them, including the neurogenesis regulator miR-132, also directed against AChE-S. Our findings point at the AChE-R splice variant as particularly susceptible to miR regulation, highlight those biological functions of cholinesterases that are likely to be subject to miR post-transcriptional control, demonstrate the selectivity of miRs in regulating specific biological processes, and open new venues for targeted interference with these specific processes.

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