

miR-3099 promotes neurogenesis and inhibits astrogliogenesis during murine neural development

ABSTRACT

MicroRNA-3099 is highly expressed during neuronal differentiation and development of the central nervous system. Here we characterised the role of miR-3099 during neural differentiation and embryonic brain development using a stable and regulatable mouse embryonic stem cell culture system for miR-3099 expression and in utero electroporation of miR-3099 expression construct into E15.5 embryonic mouse brains. In the in vitro system, miR-3099 overexpression upregulated gene related to neuronal markers such as Tuj1, NeuN, Gat1, vGluT1 and vGluT2. In contrast, gene related to astrocyte markers (Gfap, S100 β and Slc1a3) were suppressed upon overexpression of miR-3099. Furthermore, miR-3099 overexpression between E15.5 and E18.5 mouse embryonic brains led to disorganised neuronal migration potentially due to significantly decreased Gfap⁺ cells. Collectively, our results indicated that miR-3099 plays a role in modulating and regulating expression of key markers involved in neuronal differentiation. In silico analysis was also performed to identify miR-3099 homologues in the human genome, and candidates were validated by stem-loop RT-qPCR. Analysis of the miR-3099 seed sequence AGGCUA against human transcriptomes revealed that a potential miRNA, mds21 (Chr21:39186698-39186677) (GenBank accession ID: MK521584), was 100% identical to the miR-3099 seed sequence. Mds21 expression was observed and validated in various human cell lines (293FT, human Wharton's jelly and dental pulp mesenchymal stem cells, and MCF-7, MDA-MB-231, C-Sert, SW780, RT112, 5637, EJ28 and SH-SY5Y cells), with the highest levels detected in human mesenchymal stem cell lines. The analysis validated mds21 as a novel miRNA and a novel homologue of miR-3099 in the human genome.

Keyword: Embryonic stem cell; Gfap; Neuronal differentiation; Tuj1; miR-3099; miRNA homologue