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, S100β 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