The expression profile of miR-3099 during neural development of Ts1Cje mouse model of down syndrome

ABSTRACT

MicroRNA-3099 (miR-3099) plays a crucial role in regulating neuronal differentiation and development of the central nervous system (CNS). The miR-3099 is a pro-neuronal miRNA that promotes neural stem/progenitor cell (NSPC) differentiation into neuronal lineage by suppressing astrogliogenesis. Down syndrome (DS) brain exhibited increased astrogliogenesis and reduced neuronal cell density. The involvement of miR-3099 in the neurodevelopment of DS has not been investigated and potentially responsible for the neurogenic-to-gliogenic shift phenomenon observed in DS brain. To investigate the role of miR-3099 during DS brain development, neural/progenitor cell proliferation and differentiation, we profiled miR-3099 expression level in the Ts1Cje, a mouse model for DS. We analysed the Ts1Cje whole brain at embryonic day (E) 10.5, E14.5 and P1.5, proliferating neurospheres and differentiating neurospheres at 3, 9 and 15 days in vitro (DIV). Expression of miR-3099 in both the developing mouse brain and the differentiating neurosphere was not significantly different between Ts1Cje and wild type controls. In contrast, the expression level of miR-3099 was significantly higher ($p<0.05$) in proliferating NSPC derived from the Ts1Cje compared to wild-type. Further molecular profiling of NPSC and glial cell markers indicated that the expression of Sox2 ($p<0.01$) and Gfap ($p<0.05$) were significantly downregulated in Ts1Cje neurospheres as compared to that of wild type, respectively. While there were no significant differences in Tuj1 and Nestin expression levels between the Ts1Cje and wild type neurospheres, their expression levels were ~3-fold upregulated and ~2.6 downregulated Ts1Cje group, respectively. The findings suggest that dysregulation of miR-3099 affects NSPC lineage commitment as indicated by altered postmitotic neuronal cell markers. Further molecular characterisation and gene expression profiling of other neuronal and glial markers will help refine the analysis of gene-gene interactions underlying the neuropathologies of DS.

Keyword: MiR-3099; Ts1Cje; Down syndrome; MicroRNA