miR-27a inhibits maturation of oligodendrocyte precursor cells to mature oligodendrocytes

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Background

Micro RNAs (miRNAs) are short non-coding RNAs that regulate gene expression at the posttranscriptional level by complementary binding to 3'UTR regions of target genes. Modulation of gene expression by miRNAs plays a central role in neurodegenerative diseases. Recently, miRNA expression within cerebrospinal fluid (CSF)/serum/plasma has been reported to be correlated with a neurological disability or disease progression in multiple sclerosis (MS) patients. However, functional validation of individual miRNA is missing which may hold therapeutic potential.

Aim

In this study, we aimed to investigate miR-27a expression in progressive MS brain and analyze its functional role in myelination.

Methods

miRNAs expression validation and target gene regulation were confirmed by reverse transcriptase quantitative polymerase chain reaction (RT-qPCR), immuno-in situ hybridization and miRNA-3'UTR binging assay, respectively. Role of miR-27a in myelination was evaluated using in vitro primary rodent oligodendrocyte precursor cells (OPCs) culture.

Results

miR-27a expression was significantly downregulated in chronic demyelinated MS lesions validated by RT-qPCR and immuno-in situ hybridization. In vitro functional assay shows that transient transfection of chemically synthesized miR-27a-3p (mimic) in OPCs/ oligodendrocytes (OLs) inhibits differentiation and maturation of OPCs into mature OLs. Intriguingly, miR-27a overexpression stalled OPCs in the precursor stage and caused a significant increase in levels of Chondroitin sulfate proteoglycan 4 (Cspg4/Ng2) protein without an increase in OPCs proliferation. Transcriptome profiling

of miR-27a overexpressing OPCs identified several genes critical for myelination and Wnt- β-catenin signaling pathway.

Conclusions

Taken together, our results indicate that miR-27a may play a major role in arresting OPCs in the immature state leading to failure in remyelination in chronic demyelinated lesion progressive MS brain.

Keywords: Micro RNAs, multiple sclerosis, oligodendrocyte, remyelination.

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