Evidence for methylation changes in CD4+ T cells and brain tissue of multiple sclerosis (MS) patients and healthy controls (HC) strongly suggests a role for epigenetics in disease pathogenesis. We here sought to identify methylation changes in one of the key players in MS disease, CD4+ T cells, between MS patients and HC. The CD4+ T cells were sorted using a MoFlow sorter from peripheral blood mononuclear cells (PBMCs) isolated from MS cases and HC. DNA extracted from the CD4+ T cells was subjected to genome-wide DNA methylation quantification using Illumina Infinium Human Methylation 450K bead chip. The top scoring changes in DNA methylation between groups were confirmed using bisulfite pyrosequencing and miRNA expression was detected by TaqMan microRNA-assay. Preliminary analyses of the genome-wide methylation data revealed higher methylation rate at all CpG positions of the miR-21 gene in MS patients compared to controls. In line with this finding there was a lower miR-21 expression in these patients as methylation is generally associated with gene silencing. We further investigated the involvement of miR-21 in EAE, the inflammatory response will be characterized in miR-21−/− animals and littermate controls during the course of EAE. doi:10.1016/j.jneuroim.2014.08.301

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In situ microRNA profiles of astrocytes in the context of ischemic brain injury and multiple sclerosis

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Anatomic distribution is an important factor that impacts on the functional properties of astrocytes under pathologic conditions. Micro-RNAs (miRNAs) are small ribose nucleic acid (RNA) molecules that function as post-transcriptional regulators of gene expression. Distinct miRNA profiles have been associated with pro-inflammatory and anti-inflammatory responses. In this study, we analysed inflammation-related miRNA expression profiles of human glial fibrillary acidic protein (GFAP)-immunoreactive cells laser-capture microdissected from brain samples of adults with multiple sclerosis (MS) and ischemic infarcts or from control brains (with no specific pathology). When comparing miRNA profiles of astrocytes isolated from grey and white matter regions of control cases, we found differences in relative expression of specific miRNAs that have previously been detected in human astrocytes in vitro: MiRNA-125b and miRNA-338 were upregulated in white matter astrocytes, while miRNA-145 and miRNA-181a were upregulated in grey matter astrocytes. No differences in expression of the known proinflammatory miR-155 or the anti-inflammatory miR-146a were seen between white matter and grey matter astrocytes of these control cases. In cases of ischemic lesions, astrocyte expression of miR-155 was similar to the expression observed in control cases, whereas miR-146a expression was downregulated in both grey and white matter astrocytes of the ischemic lesions. Similarly, miR-155 expression in astrocytes captured from active MS lesions did not differ from that from controls, while their expression of miR-146a was downregulated. Our study demonstrates grey versus white matter regional differences in miRNA profiles of human astrocytes under non-pathologic conditions and selective abnormalities in the regulation of individual miRNAs involved in regulating inflammatory responses under pathological conditions. doi:10.1016/j.jneuroim.2014.08.302

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Differentially expressed microRNAs in multiple sclerosis patients alter regulatory T cells

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Multiple sclerosis (MS) is an immune-mediated demyelinating disease of the central nervous system, which results in a wide range