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Insight in miRNome of severe multiple sclerosis: Pilot study of distinctive relapse-onset MS phenotypes

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Molecular background and biomarkers of highly heterogenous and hardly predictable disease progression among relapse-onset MS patients are of high research interest. In the current pilot study, we aimed to employ next-generation sequencing to investigate the expression of whole small non-coding microRNAs (miRNome) in two groups of MS patients with highly distinctive progression phenotype: one with fast progressing, severely disabling course vs. mild course of MS, longitudinally followed 10 years. Peripheral blood mononuclear cells (PBMC) miRNome data was obtained from mild phenotype MS (n=4 patients) and progressive phenotype MS (n=5 patients), using TakaraBio SMARTer smRNA-Seq Kit on iSeq100 (Illumina). Pre-processing of raw sequencing data, quality control and miRNA differential expression analysis was performed using sRNAtoolbox pipeline. Functional interpretation of differentially expressed miRNA target genes was done in DIANA-miRPathv3.0. Tarbase v8.0 served as a resource of miRNA:gene interactions. Achieved read depth was approximately 1 million raw reads/sample, allowing detection of up to 92 mature miRNAs after genome alignment and miRbase v22 annotation. Differential expression analysis identified the significant upregulation of hsa-miR-23c (log2FC=4.29, Padj= 0.03) in progressive phenotype. Top significantly enriched KEGG pathways in hsa-miR-23c targets suggested regulation of molecular pathways involved in autoimmunity (antigen presentation, Epstein-Barr virus infection) and cancer. In conclusion, this pilot study indicates phenotype-related differences in expression of miRNAs, molecules with high regulatory and biomarker properties. Although detected in PBMC, has-miR-23c is highly expressed in the brain and target MS relevant genes such as, HLA (A, B, C), transferrin receptor, Nrf2, recently proposed to play important role in neurodegeneration.