

Category: Mitochondrial Diseases

Expression profiling and bioinformatics analysis of dysregulated microRNAs (miRNAs) in mitochondrial neurogastrointestinal encephalomyopathy (MNGIE).

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Background:

MNGIE is a rare and fatal inherited metabolic disorder due to a mutation in the nuclear *TYMP* gene leading to a deficiency in the enzyme thymidine phosphorylase. This subsequently causes an accumulation of the deoxynucleosides, thymidine, and deoxyuridine in tissues and body fluids, imbalances in the mitochondrial deoxyribonucleoside triphosphate pools and ultimately mitochondrial failure. The understanding of the precise molecular mechanisms of this effect and how it influences disease phenotype is poorly understood. MicroRNAs are a class of small non-coding RNAs that regulate gene expression at the posttranscriptional level. The aberrant expression of miRNAs is implicated in a wide range of diseases; their study thus offers an approach to the elucidation of the underlying molecular mechanisms of disease pathology.

Aims:

To examine the expression profile of patient serum and serum derived exosomes with the aim of providing insight into the biochemical derangements which underlie the MNGIE phenotype.

Methods:

MicroRNA was extracted from patient and healthy control serum and serum-derived exosomes and profiled using Exiqon's miCURY qPCR panel array. Differentially expressed miRNAs were subjected to bioinformatical analysis.

Results:

Compared to healthy controls, 53 and 22 up-regulated miRNAs were identified in patient serum and serum-derived exosomes, respectively. Cellular pathway enrichment analysis of the predicted target genes revealed over-representation of 8 pathways in serum, including the T cell receptor, adipocytokine, calcium and MAPK signalling pathways. In exosomes, the Jak-STAT signalling pathway was over-represented. A multiple miRNA target analysis revealed 8 and 6 predicted genes targets in serum and exosomes, respectively that were regulated simultaneously by 5 or more upregulated miRNAs.

Conclusion:

Expression profiling and bioinformatics analysis of serum-based miRNAs provides a powerful approach for elucidating potential gene targets and target pathways that are affected by deregulated miRNAs.