Diagnostic prospects of early Alzheimer's disease based on blood microRNAs

K. Zoltowska[1], S. Nagaraj[1], K. Laskowska-Kaszub[1], K. Debski[2], J. Wojsiat[1], M. Dabrowski[2], T. Gabryelewicz[3], J. Kuznicki[4], U. Wojda[1]
[1]*Neurobiology Center, Laboratory of Preclinical Testing of Higher Standard, Nencki Institute of Experimental Biology of Polish Academy of Sciences, Poland*
[2]*Neurobiology Center, Laboratory of Bioinformatics, Nencki Institute of Experimental Biology of Polish Academy of Sciences, Poland*
[3]*Department of Neurodegenerative Disorders, Mossakowski Medical Research Center, Poland*
[4]*Laboratory of Neurodegeneration, International Institute of Molecular and Cell Biology, Poland*

Alzheimer's disease (AD) is the most common cause of dementia in the elderly. One of the major challenges in the AD field is deciphering the molecular signatures, characteristic of early stages of the disease, in peripheral tissues in patients suffering from mild cognitive impairment (MCI) due to AD. In this study qRT-PCR was applied to evaluate microRNA (miRNA) profiles in blood plasma collected from 15 MCI-AD patients, whose diagnoses were confirmed by cerebrospinal fluid (CSF) biomarkers, 20 AD patients and 15 non-demented, age-matched individuals (CTR). 179 plasma miRNAs were compared between AD and CTR, and between MCI-AD and CTR. 23 differentially expressed miRNAs reported earlier as AD biomarker candidates in blood were confirmed in the current study and 26 novel differential miRNAs between AD and CTR were detected. TargetScan, MirTarBase and KEGG database analysis of 15 miRNAs that presented statistically significant differences in their expression indicated that these may regulate the expression of microtubule associated protein tau (MAPT), proteins involved in amyloid precursor protein (APP) processing and proteins regulating apoptosis. The potential of these 15 miRNAs to be used as biomarkers was further verified in independent AD, MCI-AD and CTR groups. Finally, 6 miRNAs (3 novel in AD context and 3 reported) were selected as the most promising biomarker candidates differentiating early AD from controls with the highest fold changes (from 1.32 to 14.72), consistent significance, specificities from 0.78 to 1 and sensitivities from 0.75 to 1), (patent pending, PCT/IB2016/052440). The miRNA panel is promising for diagnostics of early AD.