

BIOMARKERS (NON-NEUROIMAGING)

miRNAs in Cerebrospinal Fluid Associated with Alzheimer's Disease: a Systematic Review and Pathway Analysis

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Abstract

Background: Approximately 55 million people live with dementia, and 10 million cases are diagnosed each year worldwide (1). Alzheimer's disease (AD) is the most common type of dementia and accounts for 60% - 70% of reported cases (1). MicroRNAs are small non-coding RNAs that present highly conserved sequences, involved in gene modulation and several molecular mechanisms (2). The miRNAs can be found in cerebrospinal fluid (CSF) and they are potential biomarkers for AD diagnosis (3). This study aimed to perform a systematic review about the expression of miRNAs in the CSF of AD patients compared to cognitive controls and carry out an analysis of the biological pathways regulated by these miRNAs

Method: A systematic literature search was performed in Medline/PubMed, the Cochrane Central Register of Controlled Trials, Scopus, Lilacs, Web of Science, Embase and gray literature, including observational studies that evaluated patients with AD and healthy individuals, which evaluated the miRNA expression in CSF. To verify the main signaling pathways regulated by the miRNAs, the software Gene Cards was used (table 1).

Result: 2060 studies were retrieved and, after removing duplicates and reading titles, abstracts and full text, 26 studies met the inclusion criteria. We identified 171 differentially expressed miRNAs between AD and controls. Among them, the miRNAs -125b, -125-5p, -138-5p and -485-5p presented differentiated expression between the groups commonly in these studies. The evaluation of signaling pathways showed that regulation of gene expression, cell proliferation, and gene silencing, are regulated by these miRNAs.

Conclusion: Our results suggest that the miRNAs -125b, -125-5p, -138-5p and -485-5p are involved in AD-related biological pathways and are potential CSF biomarkers to AD diagnosis.

1. DEMENTIA. World Health Organization, 2022. Available at: <https://www.who.int/news-room/fact-sheets/detail/dementia>. Access at 21 jan. 2023.

2. CORREIA DE SOUSA, Marta et al. Deciphering miRNAs' action through miRNA editing. *International Journal of Molecular Sciences*, v. 20, n. 24, p. 6249, 2019.
3. TAKOISIS, Petros et al. Differential expression of microRNAs in Alzheimer's disease brain, blood, and cerebrospinal fluid. *Alzheimer's & Dementia*, v. 15, n. 11, p. 1468-1477, 2019.

ID Pathways	Pathways and interactions	miRNA
GO:0010629 3	acts_upstream_of negative regulation of gene expression	miRNA- 125b
GO:0010629 3	involved_in negative regulation of gene expression	miRNA-125-5p
GO:0035195 3 5	involved_in miRNA-mediated gene silencing	miRNA-485-5p
GO:0008285 3	involved_in negative regulation of cell population proliferation	miRNA-138-5p

Table 1: Relationship between regulated miRNAs and the pathways they participate.

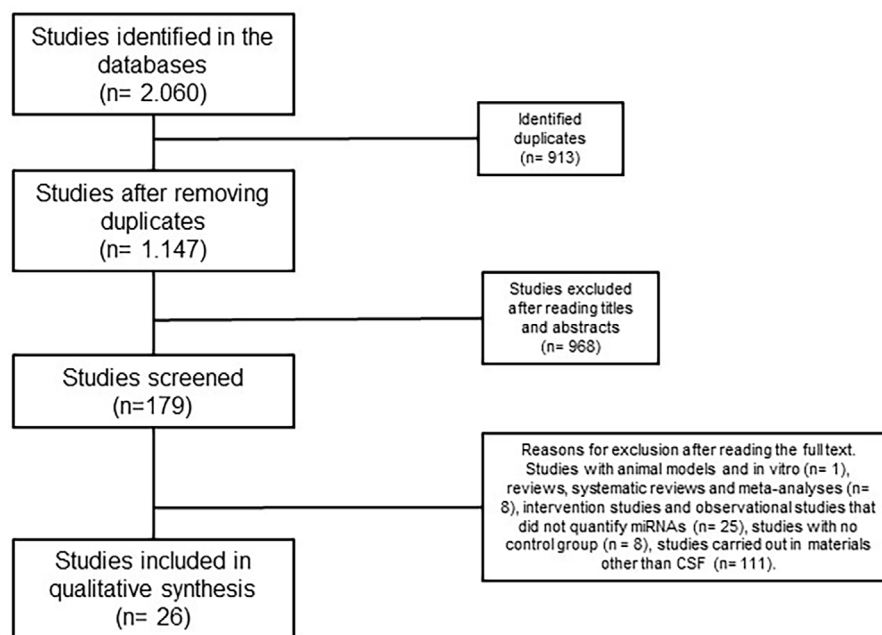


Figure 1: Flowchart of the literature search and the study selection process.