INTRODUCTION

• Alzheimer’s disease (AD) is one of the most prevalent dementia seen in elderly worldwide, with estimated one new case of AD developing every 33 seconds, and almost a million new cases every year, with prevalence of almost 13.8 million around the globe.
• The neuropathological lesions in Alzheimer’s brain consist of (a) intracellular neurofibrillary tangles, consisting of hyperphosphorylated tau protein, and (b) extracellular senile plaques containing β-amyloid.
• The main symptoms include memory loss, cognitive impairment, disorientation and psychiatric symptoms.

BIOMARKERS IN AD

• AD can be detected by measuring concentrations of protein biomarkers- total-tau, phospho-tau, and Aβ1-42 in the cerebral spinal fluid (CSF). This examination is invasive and inconvenient since CSF is obtained by lumbar punctures.
• The need of the hour is identification of new biomarkers which are less invasive and are more sensitive and specific so that early diagnosis is facilitated in the prodromal stage of dementia. Identification will further help in delaying the onset of dementia by appropriate administration of supplements.

miRNA as potential biomarkers

• MiRNAs belong to the class of non-coding RNA molecules of around 22 nt length which regulate more than 60% of all known genes through post-transcriptional gene silencing (RNAi).
• According to research carried out by Leidinger et al. (2013), dysregulation of miRNA expression in peripheral blood can serve as a potent source of diagnosis of Alzheimer’s disease and other brain related disorders.

OBJECTIVES OF THE STUDY

• To identify putative novel microRNAs in Alzheimer’s disease.
• To identify regulatory pathways which will help to elucidate the cooperative function of different miRNAs in Alzheimer’s disease.

METHODOLOGY

• Extensive literature survey and HMDD v2.0 was used to select putative miRNA in Alzheimer’s disease.
• miRTarBase, KEGG, PANTHER and GENECODIS software were used to identify and segregate the corresponding targets and the common pathways regulated by these selected miRNAs.

FLOWCHART OF WORK

• Literature survey for miRNAs in Alzheimer’s disease
• Searched HMDD v2.0 database for the upregulated and downregulated miRNAs
• Common miRNAs were selected from the literature and HMDD v2.0 database
• Ten common miRNAs were identified which were used for further analysis
• miRTarBase was referred for finding targets for the common miRNAs
• KEGG pathway database was used to find pathways for each of the miRNA targets
• PANTHER database was used to classify the targets according to their molecular functions, biological functions and protein class.
• GeneCodis was used to obtain modular and singlular enrichment analysis results.

RESULTS

LIST OF COMMON miRNAs FOUND

• miR-103b, miR-125b, miR-17 and miR-106b had maximum targets which are a part of many crucial pathways.

CONCLUSION

• The most severely affected pathway identified by our analysis was the Integrin signaling pathway.
• The other important pathways identified are Apoptosis pathway, Wnt signaling pathway, TGF-beta pathway, PDGF signaling pathway, Gonadotropin releasing hormone receptor pathway, and Inflammation mediated by chemokine and cytokine signaling pathway.

FUTURE DIRECTIONS

• Deep sequencing of miRNA together with high-throughput validation methods will complement diagnostic testing, which represents a vital step towards developing a cost effective, non-invasive and low risk diagnostic test to detect the onset and also to monitor various stages of AD.
• Circulating miRNAs are amongst the promising next generation of biomarkers for AD, and ultimately will help in the discrimination between various neurodegenerative diseases.

REFERENCES


ACKNOWLEDGEMENT

We would like to extend a sincere thanks to our director Dr. Vinaykumar B. Rale and our college Symbiosis School Of Biomedical Sciences for giving us all the facilities and funding.

CONTACT INFORMATION

• Dr. Neeti Sharma
  neeti.sharma@ssbs.edu.in
• Anshika Nikita Singh
  anshika_nikita@yahoo.co.in

Developing novel miRNA biomarkers for early detection of Alzheimer’s disease
Anshika Nikita Singh and Neeti Sharma
Symbiosis School of Biomedical Sciences
Symbiosis International University, Lavale, Pune - 412115