Blood-based biomarker for early diagnosis of Alzheimer's disease

UAB/INc/CiberNed

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PROFILE

During the last years, the basic objective of our research team has been the study of the cellular and molecular mechanisms involved in the alteration of synaptic activity and learning and memory dysfunction associated to early stages of Alzheimer's disease as a way to identify novel therapeutic targets and biomarkers for earlier diagnosis and functional recovery.

SPEAKER

Prof. José Rodríguez Alvarez has a long-lasting experience as a principal investigator in the field of neurodegeneration and in the management of academic and research teams. With extensive international collaborations, Prof. Rodríguez-Alvarez has published more than 60 research papers in international journals and has been the Principal Investigator of 18 research projects. Currently he is Group Leader in the Institute of Neurosciences (UAB), CIBERNED and visiting Professor at the Dpt Neuroscience in the Albert Einstein College of Medicine (NY, USA).

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PRODUCT

Blood-based biomarker for early diagnosis of Alzheimer's disease.

MECHANISM OF ACTION

The project deals with the development of a molecular kit blood-based for a cost-effective diagnosis of AD at early stages. This molecular kit will be based on a molecular signature obtained by the combinational analysis of plasma levels of three synaptic transmission-associated miRNAs (miR-92a-3p, miR-181c-5p and miR-210-3p).

The detection of these miRNAs by standard techniques such as RT-qPCR and RT-ddPCR will allow a specific molecular diagnosis of AD at earlier, preclinical, stages.

The levels in plasma of these three miRNAs would be a reliable biomarker for early diagnosis of AD. These miRNAs have different synaptic targets. For example, miR-92a-3p targets NRX3 (encodes for neurexin-3a) and GRIA1 (encodes for GluA1), miR-181c-5p targets NPTXR (encodes for neuronal pentraxin-1 receptor) and miR-210-3p targets NPTX1 (encodes for neuronal pentraxin-1), NPTXR, and GRINA (NMDAR-associated protein 1). All these genes, related to synaptic structure and/or function, have been shown to be down-regulated in AD human brain or in experimental models of AD.

TARGET INDICATIONS

This molecular kit could be used as a diagnostic tool in routine clinical screening and would help:

a) to provide the basis improving the non-pharmacologic therapy including the modification of lifestyle risk factors associated with AD progression.

b) to select AD patients in early stages for future clinical trials and c) to facilitate an eventual early and effective therapeutic intervention.

Early diagnosis offers also several emotional and social benefits, opening, for instance, many training, education and support programs available to individuals and family members.

CURRENT STATUS

- In our laboratory we have examined plasma levels of specific miRNAs related to synaptic proteins regulation and we have discovered and up-regulation in the expression levels of miR-92a-3p,miR-181c-5p and miR-210-3p in AD subjects.
- Moreover, we found that the mild-cognitive impairment (MCI) patients that eventually developed AD had higher plasma levels of these miRNAs compared to patients that do not progress to AD-dementia. We also found that the expression levels of these miRNAs could be specifically used as a potential biomarker for AD, as no changes in their expression levels were observed in frontotemporal dementia patients (FTD).

INNOVATIVE ASPECTS

- Nowadays there is no solution in the market for early and cost-effective diagnosis of AD. Available biomarkers, such as amyloid-β or tau detection by positron emission tomography (PET) and in the cerebrospinal fluid (CSF) have a high economical cost and require invasive procedures, making them unsuitable for routine screening.
- Blood biomarkers would provide an **easy**, minimal invasive, and **cost-reduced** method that could present a significant breakthrough in routine screening for incipient AD.
- Some companies are developing blood biomarkers for early AD based on Aβ (Pre-diagnostics AS, Norway; Araclon Biotech-Griffols, Spain; AgenT, France) or mtDNA (ADmit therapeutics, Spain).Only one company is currently developing a system based on blood miRNAs (DiamiR, USA) for eAD but, in contrast with our miRNAs signature, it does not have the potential to differentiate between mild-cognitive impairment (MCI) subjects that will or will not develop AD.

IPR

Industrial Property Rights comprises a patent family protecting not only the miRNAs combinations which are present in our diagnostic method but also all the components needed for their measurement in plasma samples and the future molecular kit that will be used for the tests. Priority patent was filed in June 2018, EP18382427.5. In 2019 the international protection was extended through the following filing: WO2019238807A1

PARTNERING OPPORTUNITIES

The TTO is leading the commercialization activities of this project. We are looking for a private partner either to continue the development of this asset through a license or collaboration agreement.