Under embargo until 11 August 2022, 05:00pm (CEST)

A new study identifies two biomarkers in the blood that better capture early signs of Alzheimer's

- **The research, led by the Barcelonaβeta Brain Research Center (BBRC), research center of the Pasqual Maragall Foundation, the Hospital del Mar Medical Research Institute (IMIM-Hospital del Mar) and the University of Gothenburg, has been published in the prestigious journal Nature Medicine.**

- **The study, which used data from almost 400 participants of the ALFA+ Study, which has the impetus of the "la Caixa" Foundation, determines that the biomarkers p-tau231 and p-tau217 measured in the blood are suitable for indicating brain changes related to the amyloid protein in people without cognitive symptoms.**

- **The results of this research make p-tau231 a very promising blood biomarker to detect early those middle-aged people who show the first brain changes associated with Alzheimer's and to conduct clinical trials aimed at this early stage of Alzheimer's.**

Barcelona, 11 August, 2022. An international team led by Dr. Marc Suárez-Calvet, researcher at the research center of the Pasqual Maragall Foundation, Barcelona Beta Brain Research Center (BBRC), and the Hospital del Mar Medical Research Institute (IMIM-Hospital del Mar), and neurologist at the Hospital del Mar, and Professor Kaj Blennow, from the University of Gothenburg, has found that the plasma biomarkers **p-tau231** and **p-tau217** are optimal for showing early signs of amyloid accumulation in the brain. The first two authors of the article, Dra. Marta Milà-Alomà and Dr. Nicholas J. Ashton, have shown that the **plasma biomarker p-tau231** is particularly suitable for capturing incipient brain changes related to the amyloid protein, before the plaque of this protein manifests itself.

The results of this analysis, supported by the "la Caixa" Foundation and the European Research Council (ERC), have been published in the prestigious scientific journal Nature Medicine, and indicate that p-tau231 is a promising blood biomarker for detecting cognitively healthy individuals at high risk of developing Alzheimer's disease. This finding will help drive clinical trials on the preclinical phase of Alzheimer's disease.

Exhaustive comparison of diagnostic accuracy

The analysis of biomarkers in the blood is an inexpensive and non-invasive procedure with a great potential to help the diagnostic process of Alzheimer's pathology and, for this reason, **the aim of the study** has been to make an exhaustive comparison between different biomarkers, since their choice could differ according to the type of test to be performed.

In collaboration with the University of Gothenburg, researchers have developed the new blood biomarker p-tau231 and compared it with five other blood biomarkers (p-tau181, p-tau217, Aβ42/40, GFAP and NfL), previously studied in the symptomatic phase of Alzheimer's disease. This is the first study to investigate all these biomarkers in the preclinical phase of Alzheimer's disease. The results show that **p-tau231 and p-tau217 are the best biomarkers in blood** to detect the first signs of amyloid accumulation in the brain. In addition, researchers have shown that higher levels of p-tau231 in the blood predict greater amyloid accumulation and cognitive loss at 3-year follow-up.

According to the research team, **the use of biomarkers in the blood could** also **facilitate clinical trials of prevention**. *"Biomarkers are a very useful tool that could speed up the development of new treatments aimed at Alzheimer's disease",* says Marc Suárez-Calvet, **head of the Biomarkers in Fluids and Translational Neurology Group at the Barcelona Beta Brain Research Center (BBRC) and researcher at the IMIM-Hospital del Mar.** *"Thanks to them, the recruitment time for participants in clinical trials on the early stage of this disease could be reduced, and the level of participation of more diverse populations would increase"*, he adds.

Abnormal levels of p-tau231

To carry out this direct comparison between the main biomarkers in plasma, the team examined their ability to detect early Alzheimer's-related brain changes in the 397 members of the Alfa+ cohort, part of the Alfa Study, which has with the support of the "la Caixa" Foundation.

The team has shown that all plasma biomarkers are altered in the preclinical phase of Alzheimer's, but they have noted **notable differences** between them. *"In the ALFA+ cohort, all the plasma biomarkers tested (p-tau181, p-tau217, p-tau231, GFAP, NfL and Aβ42/40) were significantly altered in preclinical Alzheimer's"*, explains **Marta Milà-Alomà, first author of the study and also member of the Biomarkers in Fluids and Translational Neurology Group**. *"However, plasma p-tau231 reached abnormal levels with the lowest amyloid load",* she points out.

Different biomarkers for each clinical trial

The study indicates that the blood biomarkers **p-tau231** and **p-tau217** showed the strongest association with amyloid retention in regions of early accumulation in the brain, and were associated with longitudinal increases in this protein uptake in individuals without manifest amyloid pathology at the start of the study. These **data indicate that p-tau231 and p-tau217 in plasma better capture the early brain changes** related to the presence of amyloid, even before there is a clear deposit of the amyloid protein in the form of plaques.

The results of this research make p-tau231 a **very promising blood biomarker** to detect early those middle-aged people who show the first brain changes associated with Alzheimer's and to conduct clinical trials aimed at this early stage of Alzheimer's.

Bibliographic reference

Milà-Alomà, Marta; Ashton, Nicholas J.; Shekari, Mahnaz, et al., 'Plasma p-tau231 and p-tau217 as state markers of amyloid-β pathology in preclinical Alzheimer's disease', Nature Medicine, August 11, 2022. DOI: 10.1038/s41591-022-01925-w

About Alzheimer's disease

Every 3 seconds a new case of dementia is diagnosed in the world, and it is estimated that 50 million people currently suffer from it, in most cases due to Alzheimer's. This figure translates into more than 900,000 people affected in Spain. With life expectancy on the rise, if no treatment is found to prevent or slow the course of the disease, the number of cases could triple by 2050, and reach epidemic proportions, as pointed out by latest *World Alzheimer Report 2018* published by *Alzheimer's Disease International*.

About the Barcelonaβeta Brain Research Center and the Pasqual Maragall Foundation

The Barcelonaβeta Brain Research Center (BBRC) is the research center of the Pasqual Maragall Foundation, promoted by the "la Caixa" Foundation since its creation, dedicated to the prevention of Alzheimer's disease and the study of the cognitive functions affected in healthy and pathological aging.

The Pasqual Maragall Foundation is a non-profit organization that was born in April 2008, as a response to the commitment made by Pasqual Maragall, former mayor of Barcelona and former president of the Generalitat de Catalunya, when he publicly announced that he had been diagnosed with Alzheimer's disease. The Foundation's mission is to promote research to prevent Alzheimer's and offer solutions that improve the quality of life of affected people and their caregivers.

Communication Department of the Pasqual Maragall Foundation

Barcelonaβeta Brain Research Center

Cèlia Codina Bach

ccodina@fpmaragall.org

933 160 990

Press office (ATREVIA)

Andrea Gutiérrez

agutierrez@atrevia.com

618 763 014

Communication Department of the IMIM-Hospital del Mar

Marta Calsina

mcalsina@imim.es

933 160 680

David Collantes

dcollantes@psmar.cat

600 402 785

Communication Department of the ”la Caixa” Foundation”

Andrea Pelayo

apelayo@fundaciolacaixa.org

619 74 38 29