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Genetics and Molecular Pathology Laboratory, Faculty of Medicine and Pharmacy

Nadia El Kadmiri
Hassan Ii University of Casablanca, Morocco

Neuroproteomics studies conducted in recent years have highlighted the potential involvement of the oxidoreductase, glyceraldehyde-3-phosphate dehydrogenase (GAPDH), in Alzheimer Disease (AD) associated proteins, including the β-amyloid, β-amyloid precursor. In our previous study we elucidated the critical role of GAPDH and its interaction with β-amyloid in the blood of Moroccan patients with familial AD (FAD) carrying presenilin mutations.

The aim of this current study was to assess the mechanism responsible of decreased expression of GAPDH protein in the blood of Moroccan FAD cases. Our result revealed a non-significant difference of mRNA expression level of GAPDH from FAD cases carrying mutations as compared to healthy controls and FAD case confirmed at autopsy ($P > 0.05$). Our finding is consistent with several studies by showing the direct involvement of GAPDH in amyloid aggregation; the GAPDH in AD can undergo many different oxidative post-translational modifications, which affects its chemical structure and biological activity. These Data open prospects to clarify more these mechanisms in blood of AD cases by aiming to use GAPDH as a biomarker for diagnostics and monitoring AD modification.

elkadmiri1979@gmail.com

Clathrin endocytic pathway as new player in Amyloid beta pathway

C. Matrone, Poulsen E. Toftgaard, A. Larsen, A. Zollo, A.L. Jørgensen and J.J. Enghild
Aarhus University, Denmark

The β-amyloid precursor protein (APP) has been extensively studied for its role as the precursor of the β-amyloid protein (Aβ) in Alzheimer's disease (AD). However, our understanding of the normal function of APP is still patchy. Emerging evidence indicates that a dysfunction in APP trafficking and degradation can be responsible for neuronal deficits and progressive degeneration in humans.

We recently reported that Y_{682} mutation on the $_{682\text{-}}$YENPTY$_{\text{-}687}$ domain of APP, devoted to APP internalization and trafficking (1) affects APP binding to some specific adaptors leading to an anomalous compartmentalization of APP, defects in the autophagy machinery, progressive premature neuronal degeneration and dementia in mice (2-3). A comparative Mass spectrometry analysis between mutated and control mice leaded to the identification of some crucial proteins that might be probably responsible of the phenotype observed in mutated mice (2,3). Two of these proteins, named Clathrin and its adaptor, AP2, are part of a big protein complex controlling APP trafficking inside neurons (4). Notably, the relevance of these proteins in the APP pathway and functions was further demonstrated in neuronal progenitors from Alzheimer's disease patients.

Overall, our results consolidate and refine the importance of APP adaptors in APP normal functions from an animal model of premature aging/dementia and from human differentiated stem cells. Additionally, they open the perspective to consider these adaptors as potential targets for the design and development of new therapeutic strategies.

matrone@biomed.au.dk