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Editorial

# The Intersection of Alzheimer's Disease and Protein Quality Control

**Yang Xu***

*Structural Department, TrueBinding Inc, United States*

***Corresponding Author:** Yang Xu, Structural Department, TrueBinding Inc, United States.

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Alzheimer's disease (AD) is one of the most severe neurodegenerative diseases, it progressed slowly at first and gradually gets worse [1]. AD is characterized by Amyloid-b peptide Aβ plaques and tau neurofibrillary tangles (NFTs) accumulated in the brains of patients and it is one of the leading stepwise causes of dementia cases globally [2].

Aberrant and misfolded proteins deposit in the brain of AD patients to form NFTs. Aβ is one of the NFTs which consists of a peptide contains 42/40 amino acids cleaved from the intramembrane proteolytic processing of amyloid precursor protein (APP) by β-/γ-secretase [3]. The Aβ peptides aggregate and form soluble oligomers and protofibrils-eventually subside as insoluble plaques [4]. Moreover, abnormal hyperphosphorylated tau protein is polymerized into paired helical filaments admixed with straight filaments forming neurofibrillary tangles [5]. Some other misfolded protein was described in the presence of ubiquitin by the ubiquitin protease system (UPS) in paired helical fibrils, the major components of the NFTs in AD brains [6]. The ubiquitinated protein accumulation related immunostaining is now used in diagnosing neurodegenerative diseases.

Proteins must be folded correctly to function effectively as drug targets. Over the past twenty years, the use of peptide-based therapeutics has grown exponentially Much of the research into these peptide therapeutics impacts Aβ plaques, tau plaques, and neuroreceptor signaling pathways [7]. However, there are limited treatments for this disease, this has incentivized research into AD. The autophagy-lysosomal pathway (ALP) is significant for reducing or even eliminating the misfolded proteins, invasive pathogens and dysfunctional organelles. A series of regulators of ALP, such as transcription factor EB (TFEB), have been characterized to be potential therapeutic AD targets [8]. Moreover, another potential AD target is the ATPase p97/Cdc48. This protein uses ATP hydrolysis to extract and unfold ubiquitinated proteins that are within membranes, organelles, and chromatin [9]. As p97 is critical for degrading ubiquitinated proteins and preventing aggregation, and thus, it may be a biomarker for AD with the possible future clinical application.

AD is one of the most common neurodegenerative diseases affecting people worldwide. Accordingly, these studies have led to a better understanding of this disease, nevertheless, more and more in-depth pathological and clinical studies are needed to overcome this disease [10]. It is generally accepted that AD is a protein folding disease, it is possibility to interfere with the pathogenic process would thus be to target, e.g. the aggregation of those neuron plaques. In sum, protein quality control systems (p97/Cdc48, UPS and autophagy related degradation) have evolved to deal with aggregation problems in a clearer way, maybe we should put more efforts on diversified treatments. This also leads us to have better understanding of the exact pathology with protein quality control that occur in AD.

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