Challenges and Opportunities to Address a Solution to Alzheimer's Disease

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Alzheimer's disease (AD) is the most common type of dementia and is characterized by severe neuronal losses in specific brain regions and associated with abnormal accumulation and aggregation of disease-specific proteins. Even though the pathogenesis of AD has not yet been clarified, it has been proposed that the beta amyloid peptide (Aβ), abnormal tau protein or probably both play critical role in the development of the disease leading to the formation of senile plaques and neurofibrillary tangles. The initiation of AD pathology is estimated to start several (10-15) years prior to the onset of clinical symptoms. Understanding the aggregation mechanism and how to inhibit aggregate formation is therefore crucial and will have a major impact on health along with economical ramifications worldwide.

In this presentation, recent progress in the understanding of the pathogenesis of this disease will be discussed, with emphasis on the *amyloid cascade hypothesis* and the post-translational modification of tau protein, which are the most important hypotheses in AD. These aggregate-prone proteins can undergo spontaneous self-aggregation, propagate from cell to cell, and mediate neurotoxicity. It is considered that oligomeric forms of these proteins are probably the toxic species, and there is a putative direct link between beta-amyloid peptide and tau in causing toxicity in AD. Some of the most promising therapeutic strategies currently in development for this incurable neurodegenerative disorder will be presented. In light of the suggested link between oxidative stress and neurodegeneration, it is proposed that endogenous antioxidants or dietary derived compounds may be prime candidates for anti-aggregation compounds preventing aggregation of Aβ and/or promoting clearance of Aβ aggregates. In particular, an integrated approach combining *in vitro* screening followed by *in vivo* evaluation of several bioactive antioxidants, which could lead to the development of novel aggregation inhibitors for the prevention or treatment of AD, will be described. Finally, the importance of the early detection and identification of novel potential biomarkers as the key to prevention and also to potential successful therapeutic intervention of AD will be emphasized.