Salivary Proteomics for Early Dementia Detection

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Alzheimer's Disease (AD) is the most common form of dementia and a leading cause of death in the aging population. There is currently no curative treatment for AD. Taken from its multifactorial nature, this progressive chronic disease undergoes pathogenic processes initiating long before the onset of the clinical symptoms. Hence, diagnosis is crucial to prevent and treat AD as early as possible in the disease continuum. Still to date, the definite and ultimate AD diagnosis remains the detection of amyloid-beta plaques (Aβ) and tau neurofibrillary tangles (NFT) on post-mortem brains. Currently, the golden standard for clinical diagnosis of AD consists of amyloid-beta and tau species detection in cerebrospinal fluid (CSF) and positron emission tomography (PET) biomarkers. While these diagnostic measures are highly accurate, they are invasive, costly, and typically requested after the onset of the clinical symptoms. Besides the recent advancements of blood-based biomarkers, saliva is increasingly considered as a potential alternative biofluid for non-invasive diagnostics. Thus, we performed discovery proteomics followed by ELISA and western blot procedures to analyze salivary proteome. Here we present the biochemical validation of 2 salivary biomarkers, Transthyretin (TTR) and S100 Calcium Binding Protein A8 (S100A8), which resulted in being differentially expressed in a proteomics discovery pilot. In a cross-sectional clinical cohort composed of MCI, moderate AD, and age-matched controls, we identify TTR as a potential differential diagnostic biomarker for MCI.

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