Analysis of splice variants in the proteome of Alzheimer's disease: preliminary results

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Abstract

Alzheimer's disease, Parkinson's disease and prion disease are the most common neurodegenerative diseases, affecting millions of people worldwide. Currently there is no cure or preventive therapy or quick diagnosis for any of these pathological conditions, but in all of them, abnormal accumulations of protein aggregates occur in the brain. These pathologies have been correlated to altered proteins which can be derived from alternative splicing in the pre-mRNA. Therefore, the discovery of novel protein isoforms is an important strategy to identify new biomarkers for diagnosis, potential therapeutic targets or monitoring the development of each illness. Mass spectrometry data of cerebrospinal fluid (CSF) and brain tissue from patients with Alzheimer's disease were obtained from public databases to identify the protein profile and expression of protein variants generated by alternative splicing. In the analysis of CSF data, 9 common splice variants were identified between data from patients with Alzheimer's and control patients. In addition, 4 splice variants were unique to patients with Alzheimer's disease and the canonical proteins of these genes were directly correlated with the disease as described in the literature. In the analysis of brain tissue data, we identified 16 splice variants unique to patients with Alzheimer's, which 9 canonical proteins of these genes were directly correlated this disease according to the literature. From this analysis, most alternative splicing isoforms have been identified based on proteotypic peptides which were located at junctions from non consecutive exons. The study of exclusively expressed isoforms is an important strategy for the identification of new biomarkers for the monitoring of neurodegenerative diseases.

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