EMIF Deliverable 3.3: 2 Proteomic based CSF markers for prognosis

Executive summary

In regards to CSF proteomics, we have developed and employed a new, quantification-driven proteomic approach to identify biomarkers. In contrast to the identification-driven approach, limited in scope to peptides that are identified by database searching in the first step, all MS data is considered to select biomarker candidates, which are identified in follow-up experiments.

The endopeptidome of cerebrospinal fluid from 40 Alzheimer's disease (AD) patients, 40 subjects with mild cognitive impairment, and 40 healthy controls was analyzed using multiplex isobaric labelling. Spectral clustering was used to match MS/MS spectra. The top biomarker candidate cluster (222% higher in AD compared to controls, AUC=0.97) was identified as a C-terminal fragment of pleiotrophin.

Analysis of another cohort (n=60) verified the increase in AD patients (50% higher), while no change in Parkinson's disease or progressive supranuclear palsy was observed. The identification of pleiotrophin 151-168 as a novel AD biomarker shows that a quantification-driven proteomic approach is a promising strategy for biomarker discovery.

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