

## Cerebrospinal fluid peptidomics: discovery of endogenous peptides as biomarkers of Alzheimer's disease

Neurodegenerative disorders such as Alzheimer's disease are an ever-increasing global issue, both on an individual and a societal level. A major issue in the study of neurodegeneration is the lack of diagnostic markers which has become a bottleneck in the understanding of the processes involved, as well as in the development of cures and treatments. Of particular need is biomarkers with the ability to identify individuals in the prodromal stages of neurodegeneration. Initially, this would be beneficial in the study of neurodegenerative pathogenesis but also since future treatments would be most efficient and valuable prior to cognitive and/or moto-sensory decline.

Advances in the field of bio analysis, primarily in mass spectrometry but also in chromatographic separation, may have led to analytical systems now being sufficiently sensitive for observation of the minute alterations involved in processes causing neurodegeneration.

The foundation of this thesis is the development and implementation of powerful workflows for detection, identification and quantification of endogenous peptides present in human cerebrospinal fluid. By employing a liquid chromatography-based method for reduction of CSF-complexity and a high-resolution MS for analysis we increased the known CSF-peptidome more than 10-fold. We have evaluated a chromatographic separation technique for the purpose of allowing on-line patient-to-mass spectrometer-analysis for future biomarker assays in clinical routine. Finally; we present and discuss results regarding the applicability of three novel endogenous peptide biomarker candidates for Alzheimer's disease.

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