

## **Peptidomic profiling of cerebrospinal fluid for biomarker discovery program in neurodegenerative diseases**

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Peptidomics can be define as the exhaustive study/detection of peptides in a given biological sample. Peptides in situ can schematically be sorted into biologically active peptides, including peptide hormones, and those resulting for the normal or pathologic metabolism, but without apparent physiological function. The consensus is that these peptides which are in most cases the results of proteases acting on proteins and pro-hormones in intracellular or extracellular environments, carry an exceptional biological information that we can use to find new biomarkers.

In our laboratory, we focus on the cerebrospinal fluid (CSF) peptidome in the context of neurodegenerative disorders and in particular Alzheimer disease (AD). CSF is a peculiar biological fluids that has a complexity as high as blood, but a protein concentration one hundred time lower. In addition it is available only in small quantities.

Based on the follow-up of specific peptides like the amyloid beta peptide, a known AD biomarker, we set up preanalytical procedures that preserve the peptide complexity of the samples. We then tested different pre-fractionation approach to access to low abundant entities. We finally choose a chromatographic solid phase extraction approach that allowed us to remove large and abundant proteins, and concentrate the samples for further mass spectrometry analysis. Peptides in the range of 3kD to 15kD present in complex mixture are not trivial to analyse. We choose, as a first approach, SELDI-TOF profiling which allowed us to select putative biomarkers for further validation. Finally, we checked the compatibility of our preanalytical procedures with more potent mass spectrometry analyses like LC-MS/MS.