Alzheimer’s disease (AD) is a progressive neurodegenerative disorder of complex etiology. Genetic studies of early-onset AD suggest that accumulation of amyloid-β (Aβ) peptides triggers secondary pathogenic events resulting in neuronal dysfunction and dementia in AD. The sequential cleavage of Amyloid Precursor Protein (APP) by BACE1 and γ-secretase releases Aβ peptides of variable length with Aβ1-40 being the most abundant and Aβ1-42 the most aggregation prone, toxic isoform. The concentrations of Aβ 40 and 42 peptides have already been used as biomarkers in AD and other Aβ peptides produced could also fulfil such a role.

Many different model systems are being used to study the effects of compounds targeting Aβ production and clearance in-vitro and in-vivo. Usually, Aβ peptide changes after compound intervention are quantified using existing ELISA systems specific to Aβ38, 40 and 42 as well as to Aβ1-x peptides. However, in most cases we know little about the general Aβ peptide distribution pattern in these systems beyond ELISA data and how this compares to a physiologically relevant situation. Hence the information provided by the used models is often unclear.

Combining immunoprecipitation with MALDI-TOF mass spectrometry, we have analysed a range of cell lines and primary cells including hippocampal slice cultures for their total Aβ peptide profiles. The findings were then compared to the profiles obtained from rodent brains, human cerebrospinal fluid and human brain.