Probing Amyloid Plaque Pathology in Alzheimer´s Disease using Advanced Imaging Mass Spectrometry

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Country

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Probing Amyloid Plaque Pathology in Alzheimer´s Disease using Advanced Imaging Mass Spectrometry

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The project/programme is most relevant to:

Alzheimer's disease & other dementias

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Alzheimer´s disease | Imaging Mass Spectrometry | Plaques | beta-amyloid | Lipids

Research Abstract
The major pathological hallmarks of Alzheime´s disease (AD) is the progressive accumulation and aggregation of beta-amyloid (Abeta) and hyperphosphorylated-tau, into neurotoxic deposits. Abeta aggregation has been suggested as a possibly critical, early inducer driving the disease

progression. However, the exact molecular processes underlying Abeta plaque pathology remain unknown, which hampers the development of effective AD treatment strategies. The primary goal of this project is therefore to employ advanced molecular imaging mass spectrometry (IMS) to probe the chemical and structural aspects of Abeta plaque pathology in Alzheimer´s disease. In detail, the aim is elucidate chemical properties of diffuse and mature Abeta plaques and their molecular environment in human brain tissue and transgenic mice. A further aim is to establish mechanistic insight in subcellular Abeta aggregation dynamics in transgenic AD mice using metabolic labeling and ultrahigh resolution imaging MS for elucidating spatial and temporal changes in plaque chemistry. In summary, the proposed work will help to establish the chain of molecular events that underlie amyloidogenic protein aggregation in AD pathology with a particular focus on Abeta peptide truncations and plaque- associated neuronal lipids. This will reveal potential therapeutic targets for pharmaceutical treatment of Alzheimer´s disease as well as biomarkers and theragnostic markers to monitor treatment effects.

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