

Assessing the complexity of Alzheimer's Disease with multiomic imaging on a neoflex™

Unravelling disease pathology that involves multiple molecular classes and cell types requires combining data within one workflow. This spatial multiomics example showcases a benchtop imaging mass spectrometer.

Why it matters

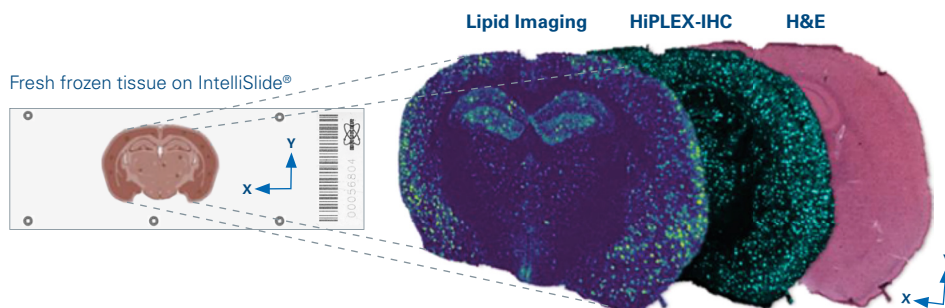
The potential of multiomic and multimodal [MALDI Imaging](#) analysis for neuropathology research is unquestioned. Contextualizing different biomolecular classes, cell types and their localization in tissue is a challenge, but it is critical for gaining insights into disease progression and providing actionable information that can lead to effective treatment options. As the large body of Alzheimer's Disease (AD) research shows, lipids and proteins provide key interactions that need to be better understood.

Methods

Sample preparation consisted of mounting fresh-frozen tissue sections of APP/PS1 mouse brain or a wild-type control mouse on IntelliSlides® and coating with matrix. Untargeted tissue imaging of lipids was carried out, followed by MS/MS of interesting lipid candidates for structure analysis directly on the tissue. After matrix removal, the same tissue section was prepared for the [MALDI HiPLEX-IHC](#) workflow following a published protocol [1]. Last, the same slide underwent H&E staining to provide tissue morphology for coregistration purposes.

Figure 1

Combination of lipid imaging data, MALDI HiPLEX-IHC data and hematoxylin & eosin (H&E) histology of the A β plaque microenvironment in Alzheimer's disease (AD) model mice.



Outcome

- Targeted protein analysis via MALDI HiPLEX-IHC staining revealed AD biomarker co-localization in the microenvironment of A β ₁₋₄₂ positive plaques in APP/PS1 mouse brain
- Correlation of lipid species revealed plaque-associated accumulation of gangliosides, LPI, PI and a depletion of two specific sulfatides
- H&E provided tissue morphology information, including the cortex and hippocampal regions as landmarks within the mouse brain tissue sample



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"This study illustrated molecular and cellular complexity in AD mouse model: Aβ peptides, lipids, activated astrocytes and microglia arguably all contribute to this disease. They can be revealed by our workflow on a single tissue section with a benchtop mass spectrometer. I'm not aware of another benchtop spatial biology instrument that can provide information on protein and lipid data layers and integrate them with histology."



Combining spatially resolved lipid information with protein biomarkers, derived from MALDI HiPLEX-IHC experiments, enables the urgently needed multimodal analyses for pathological conditions, such as AD, to gain comprehensive insight into the various molecular and cellular processes of the disease. This study demonstrates that all measurements needed for such a multimodal analysis can be accomplished on the neofleX™, a single benchtop mass spectrometer.

Representative ion images of the photocleaved mass-tag for Aβ₁₋₄₂ showing general plaque distribution in cortex and hippocampus of APP/PS1 mouse brain and manually selected ROIs containing plaques, are shown in Figure 2A. A colocalization of specific lipid species with the Aβ positive plaque regions was investigated to identify potential lipid markers (Figure 2B). Especially, GM3 and GM2 gangliosides as well as (lyso-)phosphatidylinositols show accumulation in APP/PS1 mouse brain at plaque sites. Further data evaluation revealed possible differences in lipid composition surrounding plaques. For more information see the original publication "Exploring the Aβ Plaque Microenvironment in Alzheimer's Disease Mice by Multimodal Lipid-Protein-Histology Imaging on a Benchtop Mass Spectrometer" published by Müller et al. [1].

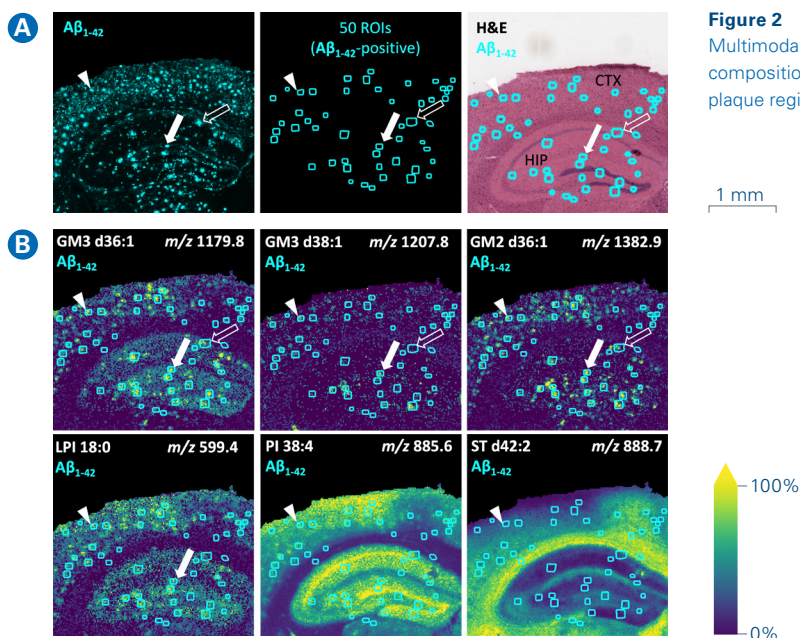


Figure 2

Multimodal MALDI Imaging reveals lipid composition of individual Aβ₁₋₄₂-positive plaque regions in AD mouse brain tissue



Reference

- [1] Müller E, Enzlein T, Niemeyer D, von Ammon L, Stumpo K, Biber K, Klein C, Hopf C (2025). Exploring the Aβ Plaque Microenvironment in Alzheimer's Disease Mice by Multimodal Lipid-Protein-Histology Imaging on a Benchtop Mass Spectrometer. *Pharmaceuticals*, **18**(2), 252; <https://doi.org/10.3390/ph18020252>

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