

# Imaging mass cytometry in understanding of biology and pathophysiology of neuronal microenvironment

## Abstract

To better understand the pathology in neurodegenerative diseases, we implemented the use of Imaging Mass Cytometry (IMC) for a highly multiplexed spatial proteomic profiling in post-mortem human brain. After staining on formalin-fixed paraffin-embedded sections using a panel of metal-conjugated antibodies, the tissue was ablated by a precisely directed laser beam then ionised before reaching an ion detector which differentiated signal from each metal tag based on differences in mass.

Here we report our workflow including panel design, antibody optimisation, image acquisition and data analysis tailored for neuroscience research. We have optimised over 50 antibodies to cover cytoarchitecture, pathology and disease mechanisms including those for glial cells, neuron, vascular and synaptic markers, as well as markers involved in pathology, inflammation and senescence. We adopted different image analysis softwares, including imageJ, Ilastik, Cell Profiler and histoCAT, to achieve an automatic and adaptive cell segmentation and subsequent cellular protein profiling. Our pipeline addresses different cell morphologies in the nervous system which are characterised by their well-formed cell processes. We also explored various cell types in the microenvironment of pathological protein aggregates and vasculature with single cell resolution.

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