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ID-2-IN-6079 Mass spectrometry imaging: approaching cellular resolution for highly specific molecular information

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Mass spectrometry imaging (MS imaging) is the method of scanning a sample of interest and generating an image of the intensity distribution of a specific analyte ion. In contrast to most histochemical techniques, mass spectrometry imaging can differentiate (amino acid) modifications and does not require labelling of compounds. Our work is focused on obtaining reliable chemical information and on increasing the spatial resolution in order to detect (sub)cellular features. Here we present a number of improvements in instrumentation, sample preparation, measurement parameters and data processing.

MS imaging experiments were performed with a high resolution atmospheric-pressure imaging source (AP-SMALDI10, TransMIT GmbH, Giessen) attached to 'LTQ Orbitrap', 'Exactive Orbitrap' or 'Q Exactive' mass spectrometers (Thermo Scientific GmbH, Bremen). Pixel size was between 2 and 10 µm. Mass accuracy was better than 2 ppm (root mean square) under imaging conditions [1,2]. Tentative identification based on accurate mass was confirmed by on-tissue MS/MS experiments.

The capabilities and characteristics of our method will be discussed on a number of applications. Phospholipids and smaller metabolites such as nucleic acids and cholesterol were imaged in single cells at 7 µm pixel size. Phospholipids were investigated in detail in human tumor biopsies. The lateral ventricle region of a coronal mouse brain section was imaged at 2 µm pixel size. Non-mammalian tissue samples often require specific sample preparation. This will be discussed on the example of metabolite imaging in plant tissue sections.

MS image analysis for all these experiments showed excellent agreement with histological staining evaluation. In addition it provided highly specific molecular information. In many cases signals with very similar mass ($\Delta m/z<0.1$) showed distinctly different distributions, which demonstrates the need for high mass resolution in order to obtain reliable information from MS imaging experiments of complex biological samples.

Newest developments in instrumentation and methodology will be demonstrated. This includes strategies for increased measurement speed, dynamic range for MS image generation of more than three orders of magnitude and simultaneous detection of positive and negative ions in one experiment.

General trends and developments in the field of mass spectrometry will be briefly discussed. This includes strategies for flexible data analysis on the basis of the data format imzML (www.imzml.org) and activities in the framework of COST action (European Cooperation in Science and Technology) „Mass Spectrometry Imaging: New Tools for Healthcare Research" (BM1104).

[1] Römpp, Guenther, Schober, Schulz, Takats, Kummer, Spengler (2010) Angew. Chem. Int. Ed. 49 (22):3834-3838.

[2] Römpp, Spengler (2013) Histochemistry and Cell Biology 139(6): 759-783.