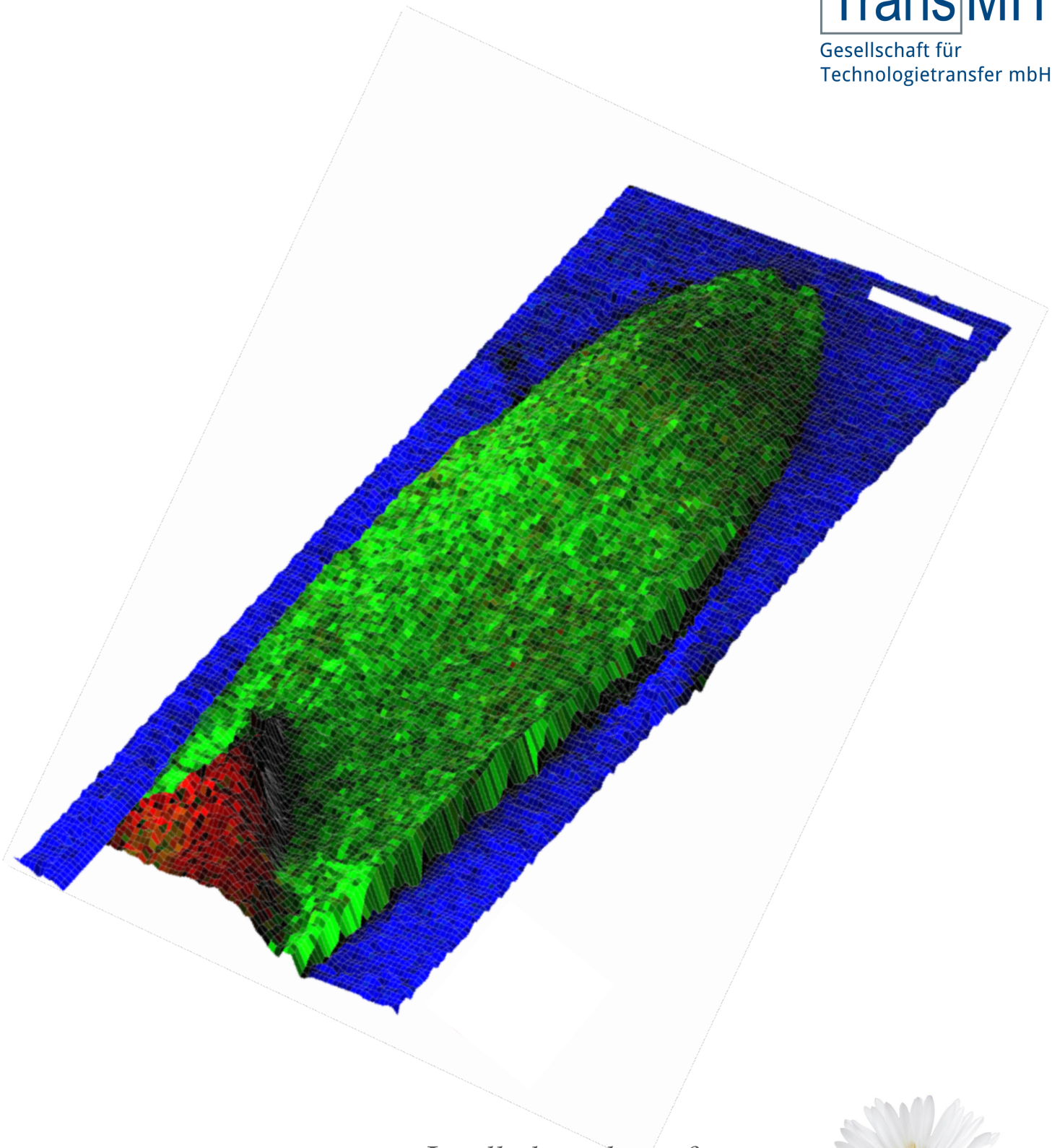
TransMIT
Gesellschaft für
Technologietransfer mbH



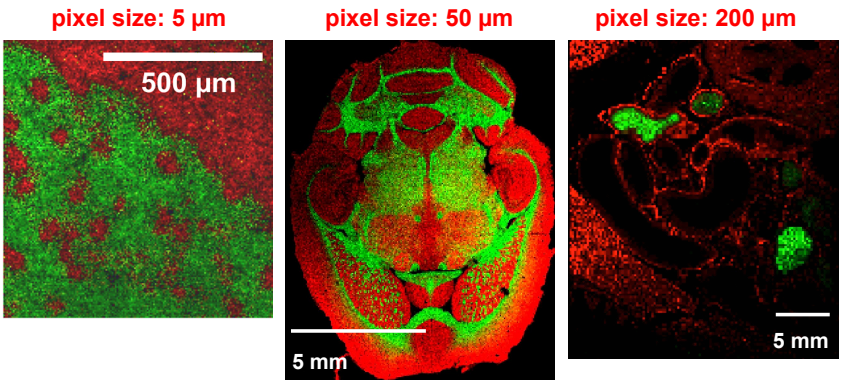
Its all about the surfaces

AP-SMALDI^5 AF

High-performance Mass Spectrometry Imaging

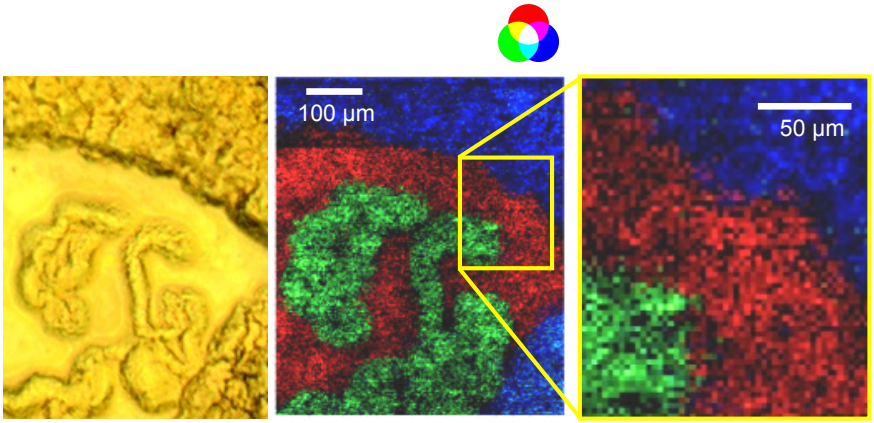
AP-SMALDI⁵ AF

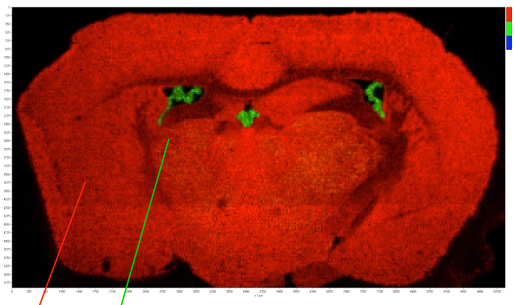
MALDI Imaging with high resolution in mass and space



Atmospheric-pressure MALDI mass spectrometry imaging at various lateral resolutions: mouse brain coronal section; mouse brain horizontal section; rat intestinal tract.

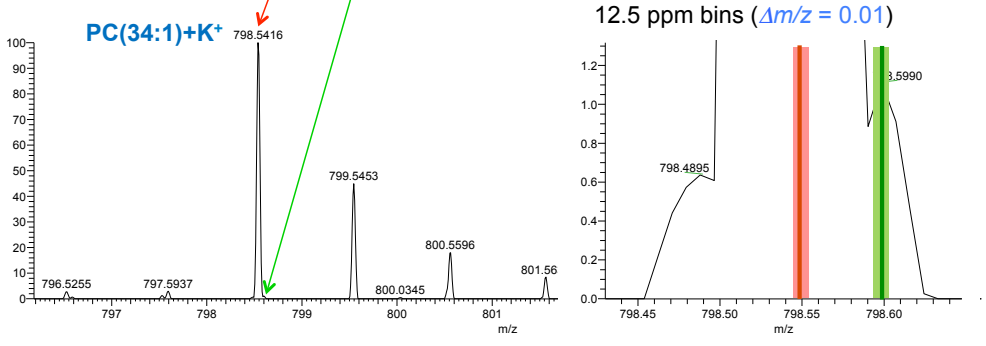
Lateral resolution (step size, pixel size) 5 µm **without oversampling**, at 3 to 5 µm ablation spot diameter. **Oversampling** analyses with smaller step sizes (pixel sizes) are also possible, with reduced quality, e.g.: mouse brain choroid plexus, **3 µm** pixel size





Choroid plexus

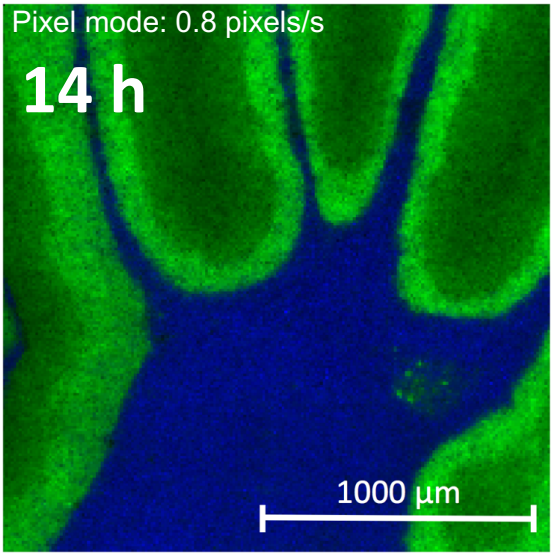
Highest imaging selectivity and dynamic range, due to orbital trapping mass analysis

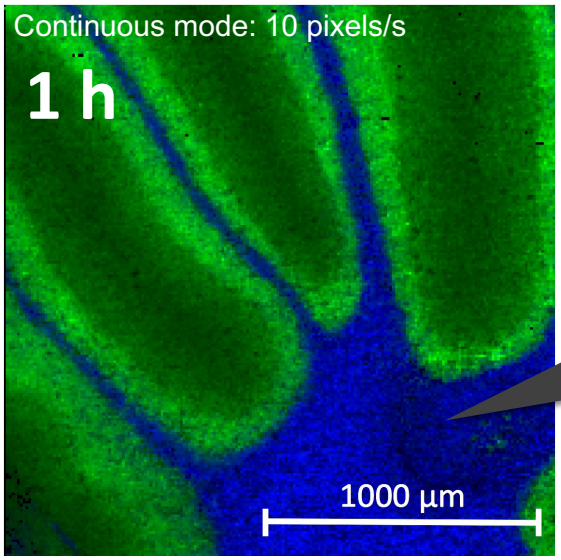


AP-SMALDI5 AF

MALDI Imaging at high laser repetition rate

High-speed mode

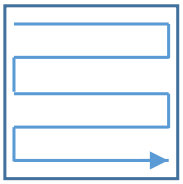


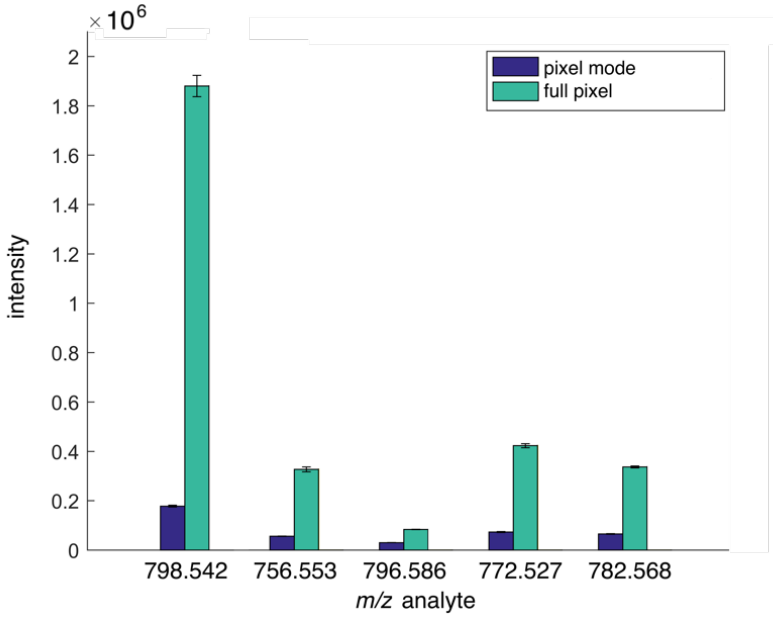


High-speed imaging in continuous scanning mode (at reduced mass resolution; actual speed depends on Orbitrap model)

Full pixel mode

En-hanced signal inten-sities by analysis of entire sample pixel area (values depend on chosen pixel size)

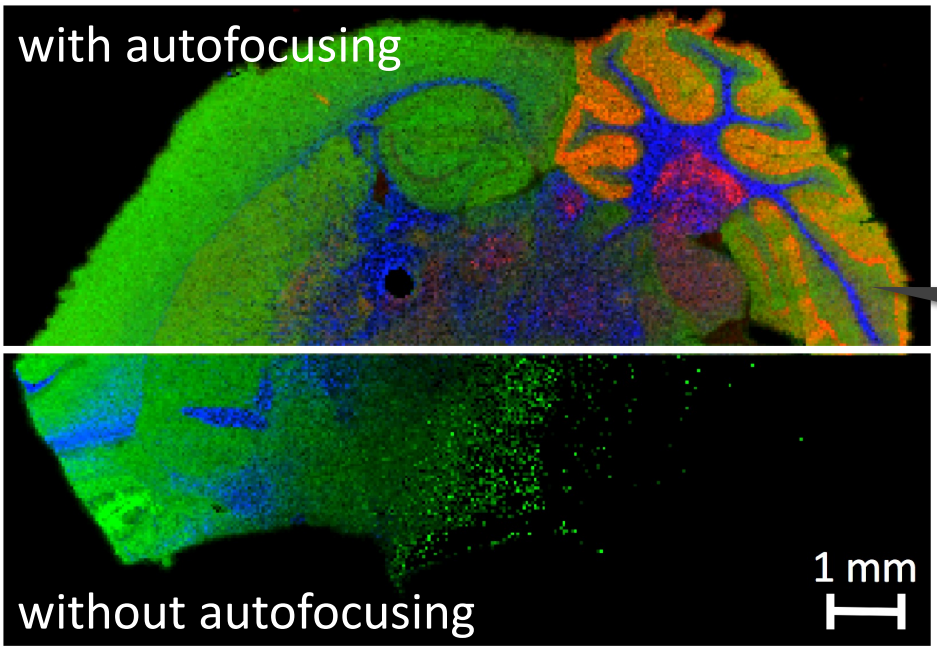




AP-SMALDI⁵ AF

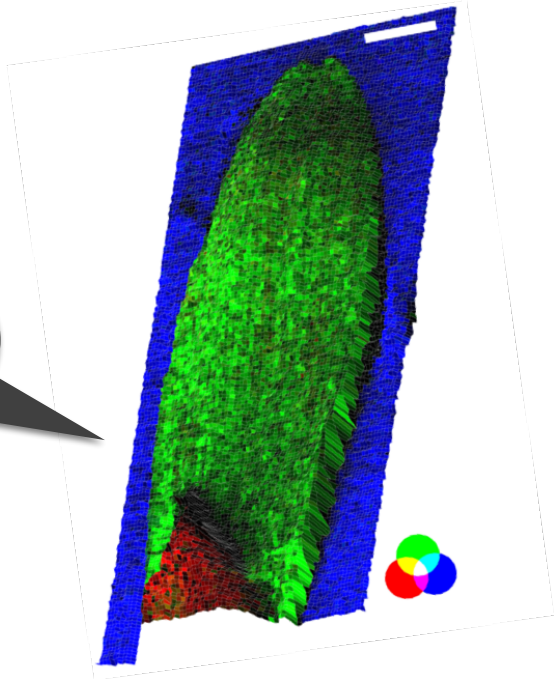
MALDI Imaging in two and three dimensions

Tilt correction

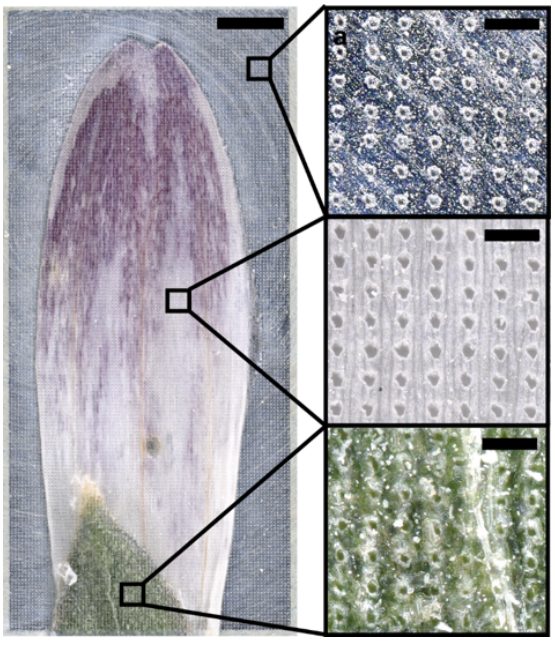


Authentic imaging of imperfect or tilted sections

3D-surface mode



3D RGB MS image of a daisy blossom



Kompauer M, Heiles S, Spengler B, Autofocusing MALDI mass spectrometry imaging of tissue sections and 3D chemical topography of nonflat surfaces. **Nature Methods** 14 (2017) 1156-1158.

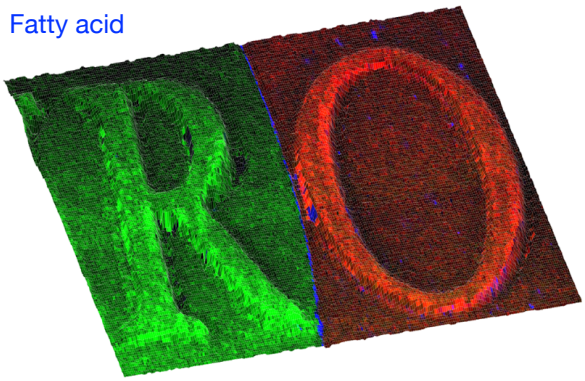
AP-SMALDI5 AF

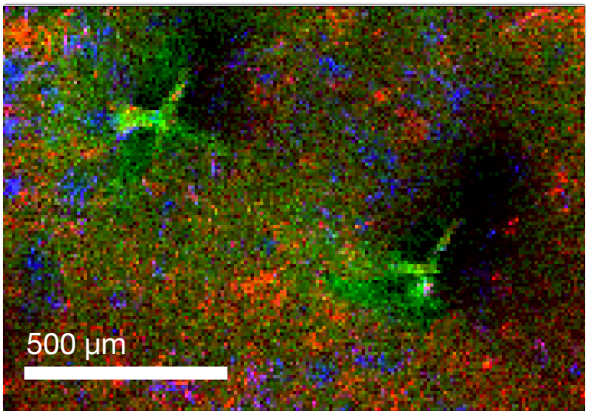
MALDI Imaging in two and three dimensions

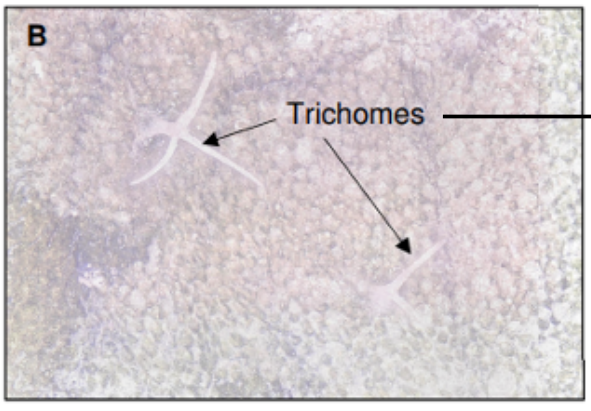
Organometallic zinc complex

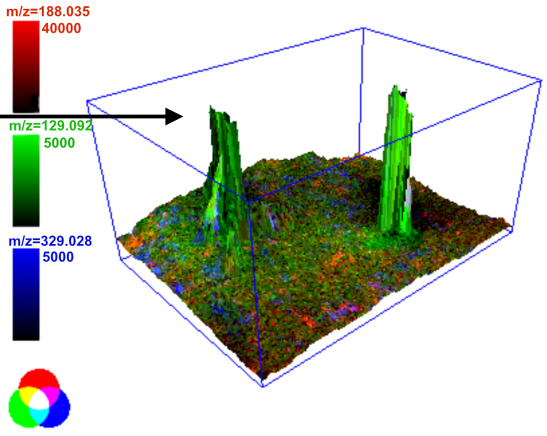
Organometallic copper/nickel complex

Fatty acid







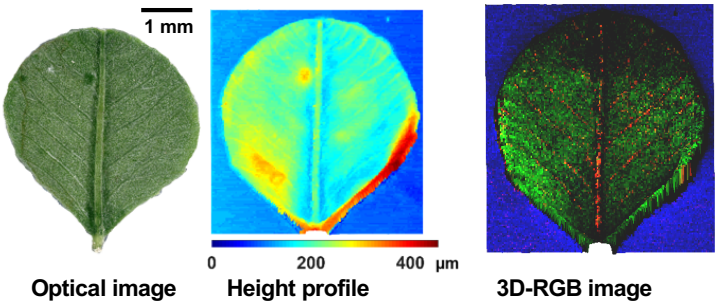


Kompauer M, Heiles S, Spengler B, Autofocusing MALDI mass spectrometry imaging of tissue sections and 3D chemical topography of nonflat surfaces. **Nature Methods** 14 (2017) 1156-1158.

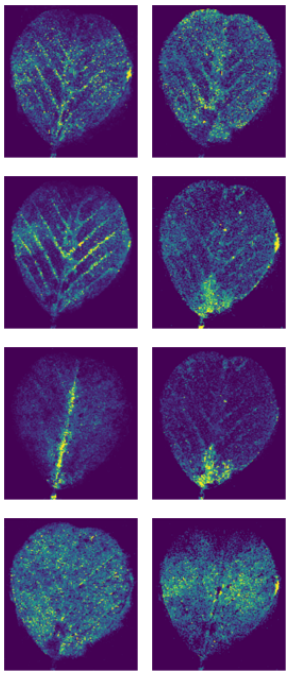
AP-SMALDI5 AF

MALDI Imaging in two and three dimensions

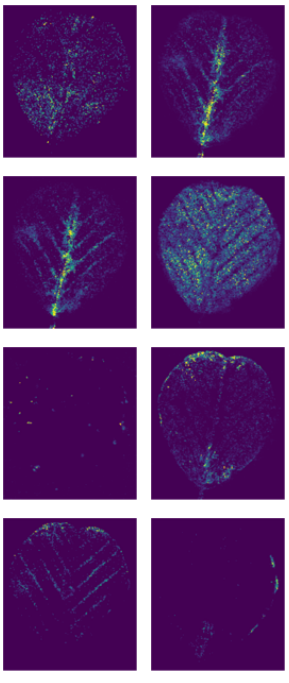
Metabolomics imaging of non-flat samples



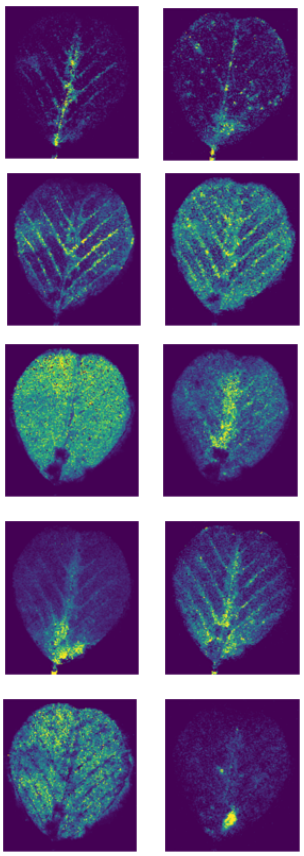
Saccharides



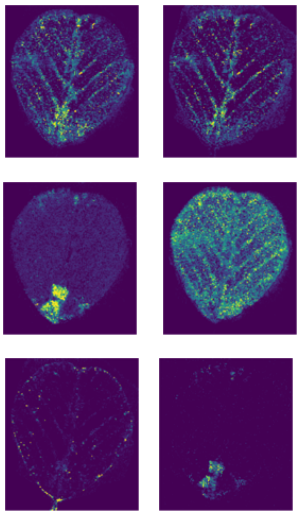
Lipids



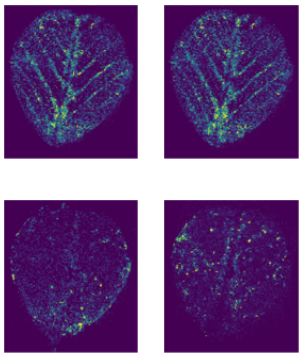
Glycosides



Flavones

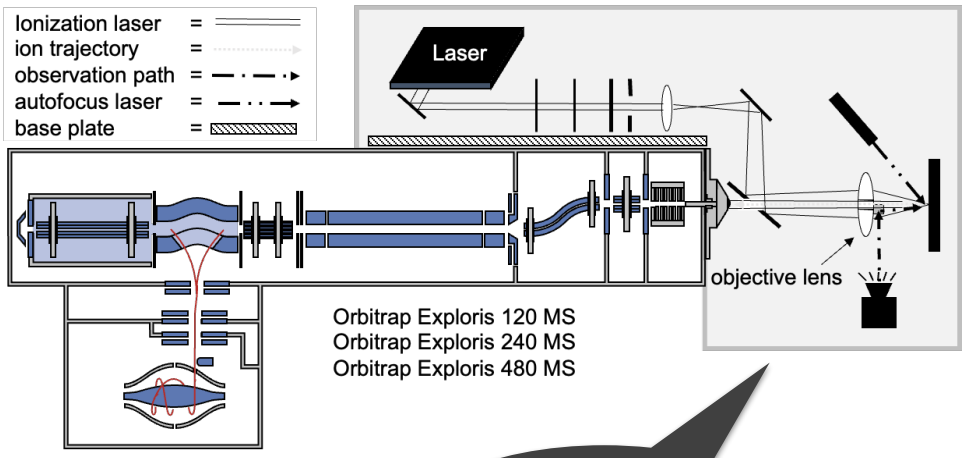


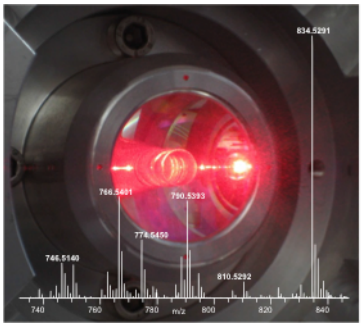
Peptides



AP-SMALDI5 AF

High resolution in mass and space

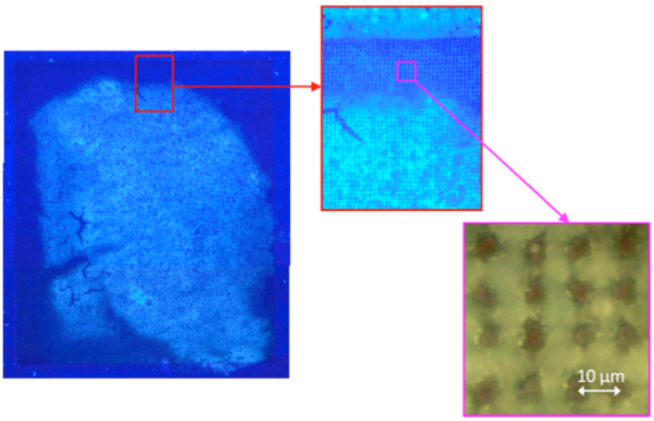




Ambient-pressure ion source for highest performance under semi-physiological conditions

Unique coaxial setup for orthogonal laser irradiation, using a centrally bored objective lens

Ablation spot size is 5 µm in diameter on tissue under typical conditions. Post-measurement histochemistry is routinely possible down to 10 µm step size.



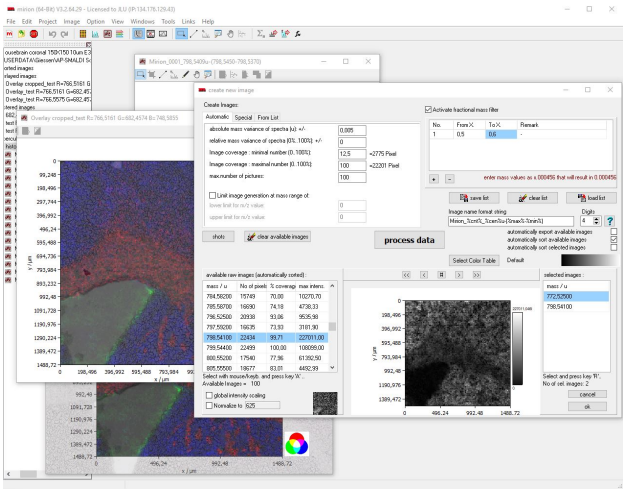
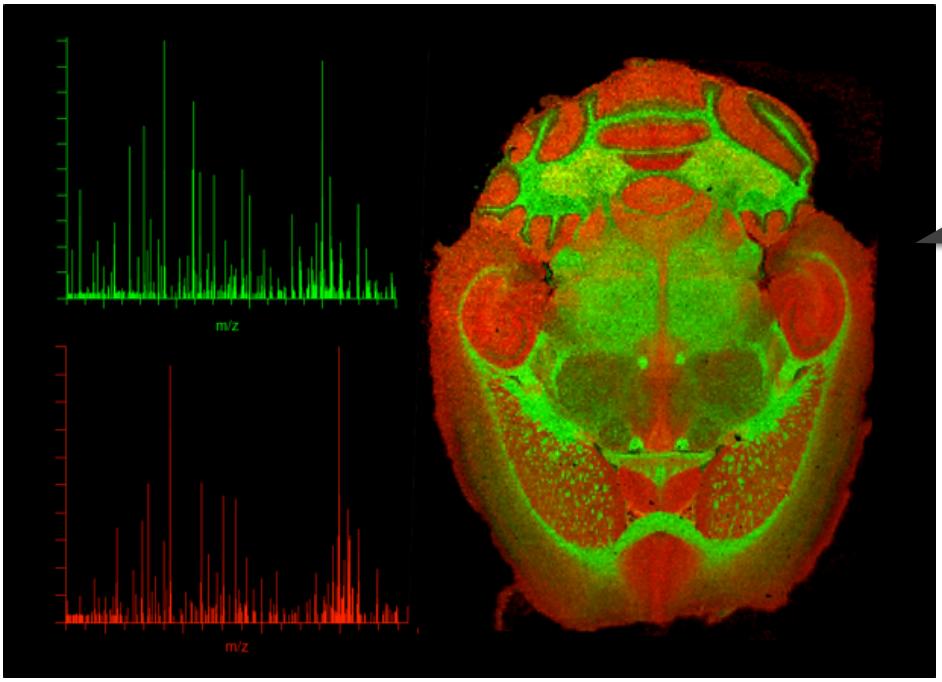


Image generation and data analysis is done with a powerful software package, including imzML integration for using open access image analysis programs.

[molecular histology]

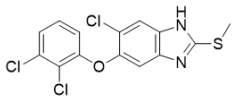


High-contrast molecular imaging of lipids, peptides, on-tissue digested proteins, small molecules, metabolites, compounds, …

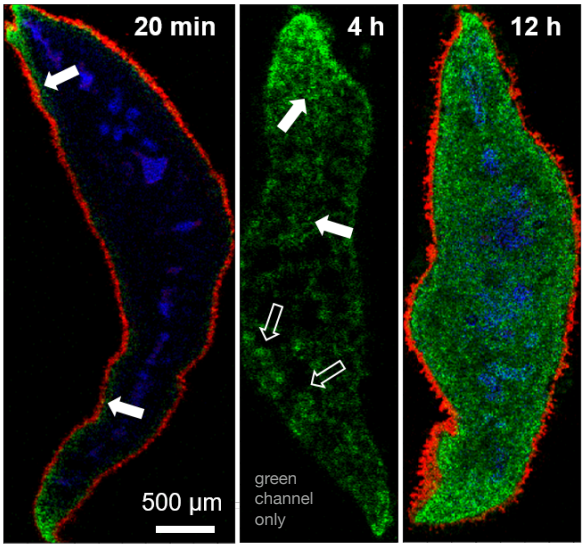
… from animal and human tissue, plants, insects, single cells, organoids, …

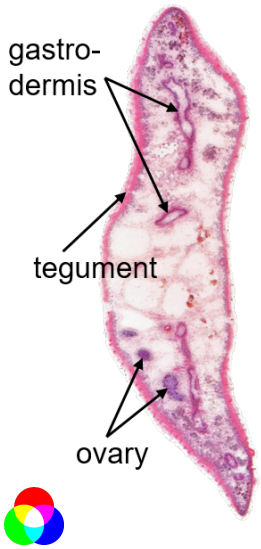
Römpp A, Spengler B, **Histochem Cell Biol** (2013) 139:759–783.

Fasciola



Triclabendazole





Uptake of exogenous drug Triclabendazole (green) in the zoonotic parasite *Fasciola hepatica* after 20 min, 4 h, and 12 h interaction time

m/z 828.5961
HexCer 38:0;O4 [M+K]$^+$

m/z 358.9571
Triclabendazole [M+H]$^+$

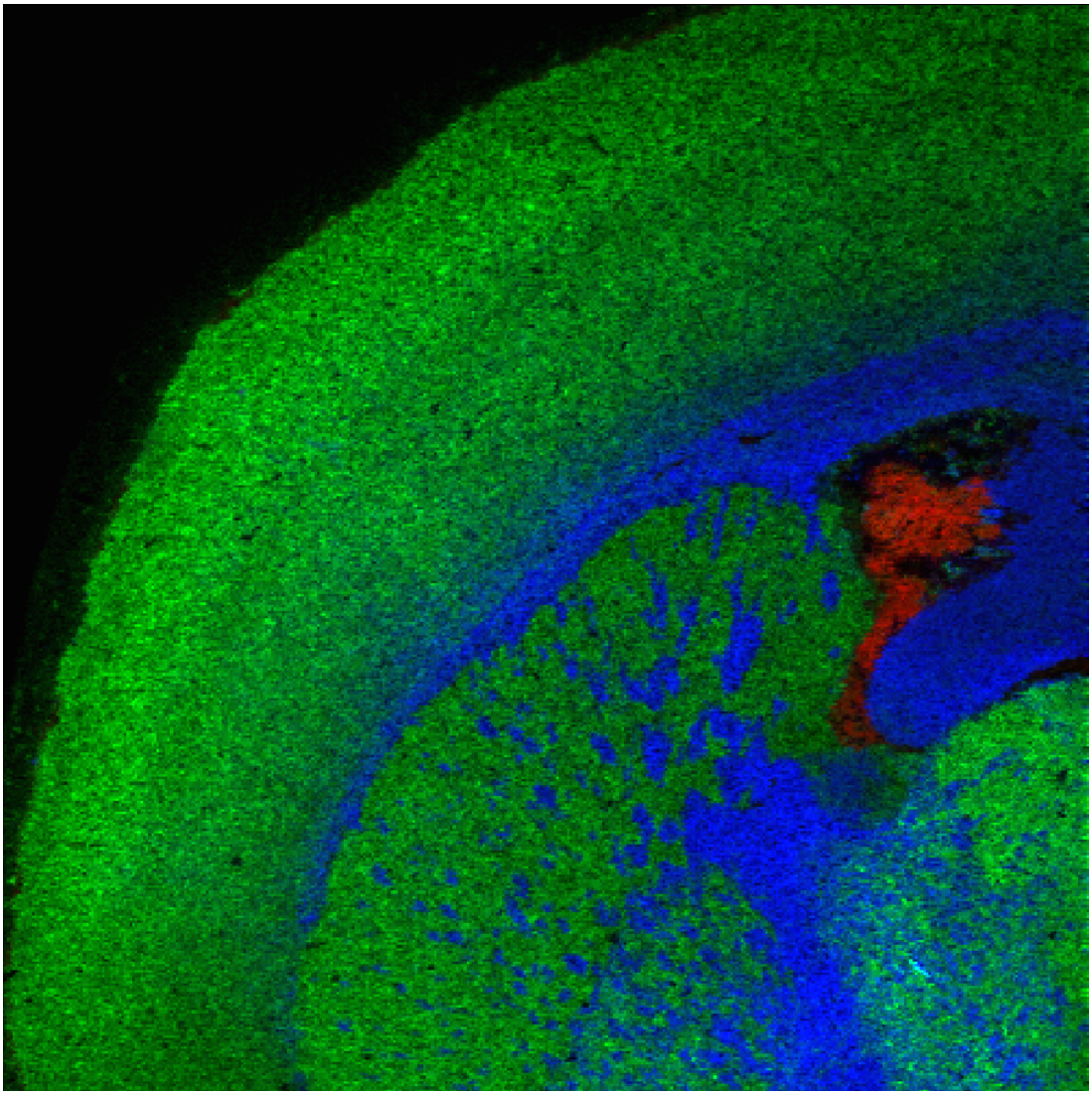
m/z 751.5039
PA O-38:3 [M+K]$^+$

Pixel size 10 µm

Morawietz CM, Houhou et al., **Front. Vet. Sci.** (2020) 7: 611270 .

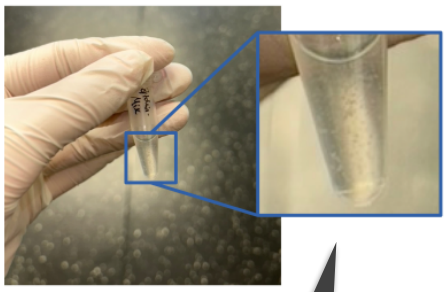
Exploring Nature

by High-Performance MALDI Mass Spectrometry Imaging



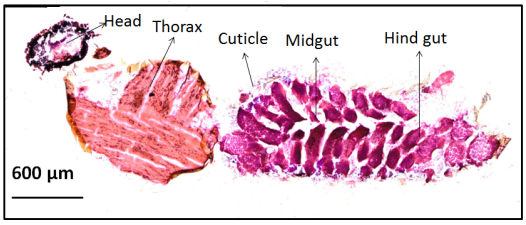
[delicate objects]

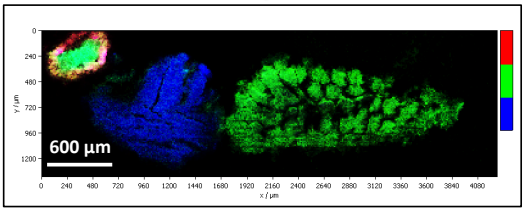
Anopheles stefensi,
body weight app. 100 µg
body length app. 3 mm



Intestinal organoids
in solution

10 µm thick section of embedded mosquito, H&E-stained after analysis

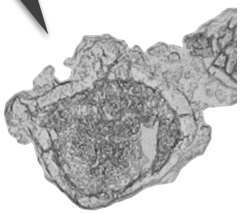


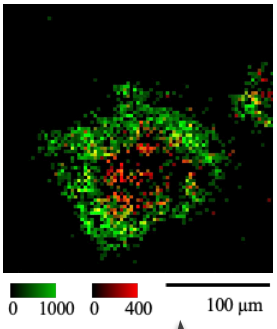


[SM (34:1)+Na]⁺ (+0.28 ppm)
[PA (38:3)+Na]⁺ (-0.08 ppm)
[PC (32:0)+Na]⁺ (+1.44 ppm)

Individual phospholipid species are characteristic for tissue types, body regions or metabolic states.

20 µm thick section of organoid, showing layer of epithelial cells and cell fragments inside the lumen



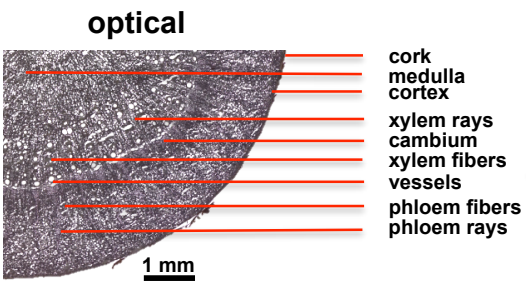


[PC (O-36:1) 774.6358 (+1.7 ppm)
[PC (34:1) 808.5816 (-1.4 ppm)

MS image (3 µm step size), depicting morphological features of the organoid

Khalil SM, Rompp A, Pretzel J, Becker K, Spengler B,
Anal Chem 87 (2015) 11309-16.

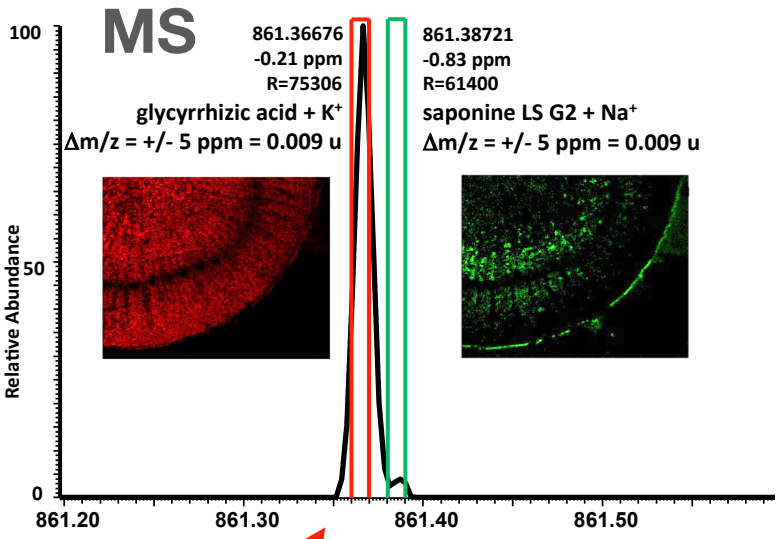
[image-assisted identification]



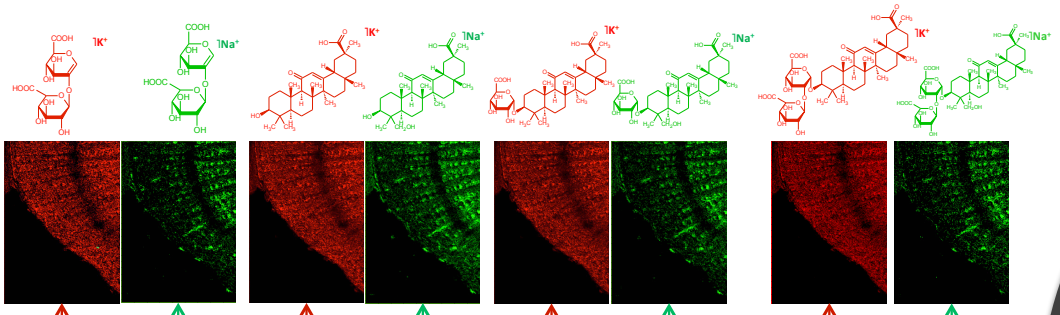
Rhizome section of licorice (*Glycyrrhiza glabra*). The plant has multiple pharmacological activities (anti-inflammatory, antimicrobial, antiviral, anti-tumor). A large number of saponines, flavonoid glycosides and free flavonoids were detected and imaged.

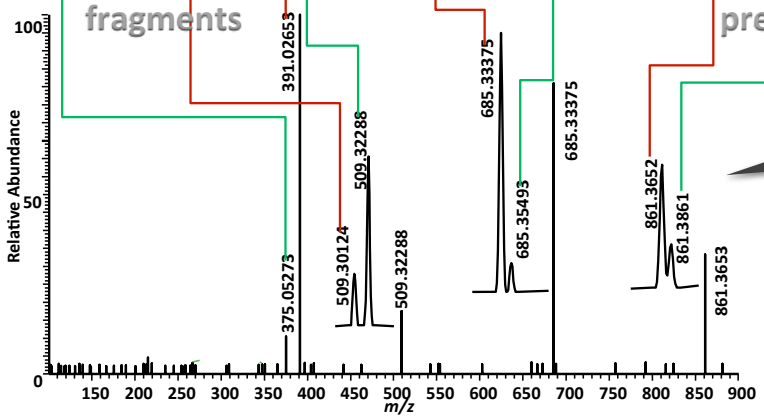
MS images and single-pixel mass spectrum of two closely neighboring natural compounds, glycyrrhizic acid (potassiated) and saponine LS G2 (sodiated), detected in the rhizome section.

The two signals differ by only 0.02 Da. The two images were generated with a *m/z* bin width of 10 ppm (green and red bars)



MS/MS





MS/MS images of glycyrrhizic acid and saponine LS G2 precursors reveal two classes of fragment ions, corresponding to the two precursor ions.

MS/MS images assist in structural characterisation and identification in complex samples. Fragment ions and their precursors have equivalent images.

The MS/MS spectrum is a single pixel spectrum selected for demonstration.

Li B, Bhandari DR, Janfelt C, Römpp A, Spengler B, **PLANT** 80 (2014) 161-171.

Selected international publications using AP-SMALDI technology

1. Bartels B, Svatos A. Spatially resolved in vivo plant metabolomics by laser ablation-based mass spectrometry imaging (MSI) techniques: LDI-MSI and LAESI. Frontiers in Plant Science. 2015;6. DOI: 10.3389/fpls.2015.00471
2. Kusari S, Sezgin S, Nigutova K, Cellarova E, Spiteller M. Spatial chemo-profiling of hypericin and related phytochemicals in Hypericum species using MALDI-HRMS imaging. Analytical and Bioanalytical Chemistry. 2015;407(16):4779-91. DOI: 10.1007/s00216-015-8682-6
3. Wang WX, Kusari S, Sezgin S, Lamshoft M, Kusari P, Kayser O, Spiteller M. Hexacyclopeptides secreted by an endophytic fungus Fusarium solani N06 act as crosstalk molecules in Narcissus tazetta. Applied Microbiology and Biotechnology. 2015;99(18):7651-62. DOI: 10.1007/s00253-015-6653-7
4. Ait-Belkacem R, Dilillo M, Pellegrini D, Yadav A, de Graaf EL, McDonnell LA. In-Source Decay and Pseudo-MS3 of Peptide and Protein Ions Using Liquid AP-MALDI. Journal of the American Society for Mass Spectrometry. 2016;27(12):2075-9. DOI: 10.1007/s13361-016-1511-0
5. Beck S, Stengel J. Mass spectrometric imaging of flavonoid glycosides and biflavonoids in Ginkgo biloba L. Phytochemistry. 2016;130:201-6. DOI: 10.1016/j.phytochem.2016.05.005
6. Eckelmann D, Kusari S, Spiteller M. Occurrence and spatial distribution of maytansinoids in Putterlickia pyracantha, an unexplored resource of anticancer compounds. Fitoterapia. 2016;113:175-81. DOI: 10.1016/j.fitote.2016.08.006
7. Kucharikova A, Kusari S, Sezgin S, Spiteller M, Cellarova E. Occurrence and Distribution of Phytochemicals in the Leaves of 17 In vitro Cultured Hypericum spp. Adapted to Outdoor Conditions. Frontiers in Plant Science. 2016;7. DOI: 10.3389/fpls.2016.01616
8. Mascini NE, Cheng ML, Jiang L, Rizwan A, Podmore H, Bhandari DR, Rompp A, Glunde K, Heeren RMA. Mass Spectrometry Imaging of the Hypoxia Marker Pimonidazole in a Breast Tumor Model. Analytical Chemistry. 2016;88(6):3107-14. DOI: 10.1021/acs.analchem.5b04032
9. Belov ME, Ellis SR, Dilillo M, Paine MRL, Danielson WF, Anderson GA, de Graaf EL, Eijkel GB, Heeren RMA, McDonnell LA. Design and Performance of a Novel Interface for Combined Matrix-Assisted Laser Desorption Ionization at Elevated Pressure and Electrospray Ionization with Orbitrap Mass Spectrometry. Analytical Chemistry. 2017;89(14):7493-501. DOI: 10.1021/acs.analchem.7b01168
10. Breindahl T, Kimergard A, Andreasen MF, Pedersen DS. Identification of a new psychoactive substance in seized material: the synthetic opioid N-phenyl-N- 1-(2-phenethyl)piperidin-4-yl prop-2-enamide (Acrylfentanyl). Drug Testing and Analysis. 2017;9(3):415-22. DOI: 10.1002/dta.2046
11. Dilillo M, Pellegrini D, Ait-Belkacem R, de Graaf EL, Caleo M, McDonnell LA. Mass Spectrometry Imaging, Laser Capture Microdissection, and LC-MS/MS of the Same Tissue Section. Journal of Proteome Research. 2017;16(8):2993-3001. DOI: 10.1021/acs.jproteome.7b00284
12. Eckelmann D, Kusari S, Spiteller M. Spatial profiling of maytansine during the germination process of Maytenus senegalensis seeds. Fitoterapia. 2017;119:51-6. DOI: 10.1016/j.fitote.2017.03.014
13. Nishidate M, Yamamoto K, Masuda C, Aikawa H, Hayashi M, Kawanishi T, Hamada A. MALDI mass spectrometry imaging of erlotinib administered in combination with bevacizumab in xenograft mice bearing B901L, EGFR-mutated NSCLC cells. Scientific Reports. 2017;7. DOI: 10.1038/s41598-017-17211-6
14. Sorensen IS, Janfelt C, Nielsen MMB, Mortensen RW, Knudsen NO, Eriksson AH, Pedersen AJ, Nielsen KT. Combination of MALDI-MSI and cassette dosing for evaluation of drug distribution in human skin explant. Analytical and Bioanalytical Chemistry. 2017;409(21):4993-5005. DOI: 10.1007/s00216-017-0443-2
15. Wenande E, Olesen UH, Nielsen MMB, Janfelt C, Hansen SH, Anderson RR, Haedersdal M. Fractional laser-assisted topical delivery leads to enhanced, accelerated and deeper cutaneous 5-fluorouracil uptake. Expert Opin Drug Deliv. 2017;14(3):307-17. DOI: 10.1080/17425247.2017.1260119
16. Eckelmann D, Spiteller M, Kusari S. Spatial-temporal profiling of prodiginines and serratamolides produced by endophytic Serratia marcescens harbored in Maytenus serrata. Scientific Reports. 2018;8. DOI: 10.1038/s41598-018-23538-5
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