



HAL
open science

BRAIN GLYCEROPHOSPHOLIPIDS AND CHOLESTEROL IMAGING BY MASS SPECTROMETRY

Anne Héron, Vanessa W Petit, Alexandre Seyer, Farida Benabdellah, David
Touboul, Alain Brunelle, Olivier Laprèvote

► **To cite this version:**

Anne Héron, Vanessa W Petit, Alexandre Seyer, Farida Benabdellah, David Touboul, et al.. BRAIN GLYCEROPHOSPHOLIPIDS AND CHOLESTEROL IMAGING BY MASS SPECTROMETRY. 1ère Journée de l'Institut Médicament-Toxicologie-Chimie-Environnement, Apr 2010, Paris, France. hal-01609936

HAL Id: hal-01609936

<https://hal.science/hal-01609936v1>

Submitted on 14 Oct 2017

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0
International License

BRAIN GLYCEROPHOSPHOLIPIDS AND CHOLESTEROL IMAGING BY MASS SPECTROMETRY

A. Héron¹ *, V. Petit², A. Seyer², F. Benabdellah², D. Touboul², A. Brunelle², O. Laprèvote¹

¹ Laboratoire de Chimie-Toxicologie Analytique et Cellulaire, EA 4463, Faculté des Sciences Pharmaceutiques et Biologiques, Université Paris Descartes, 4 avenue de l'Observatoire 75006 Paris, France

² Centre de Recherche de Gif, Institut de Chimie des Substances Naturelles, CNRS, Avenue de la Terrasse 91198 Gif-sur-Yvette, France

* Auteur correspondant/présentateur du poster anne.heeron@parisdescartes.fr

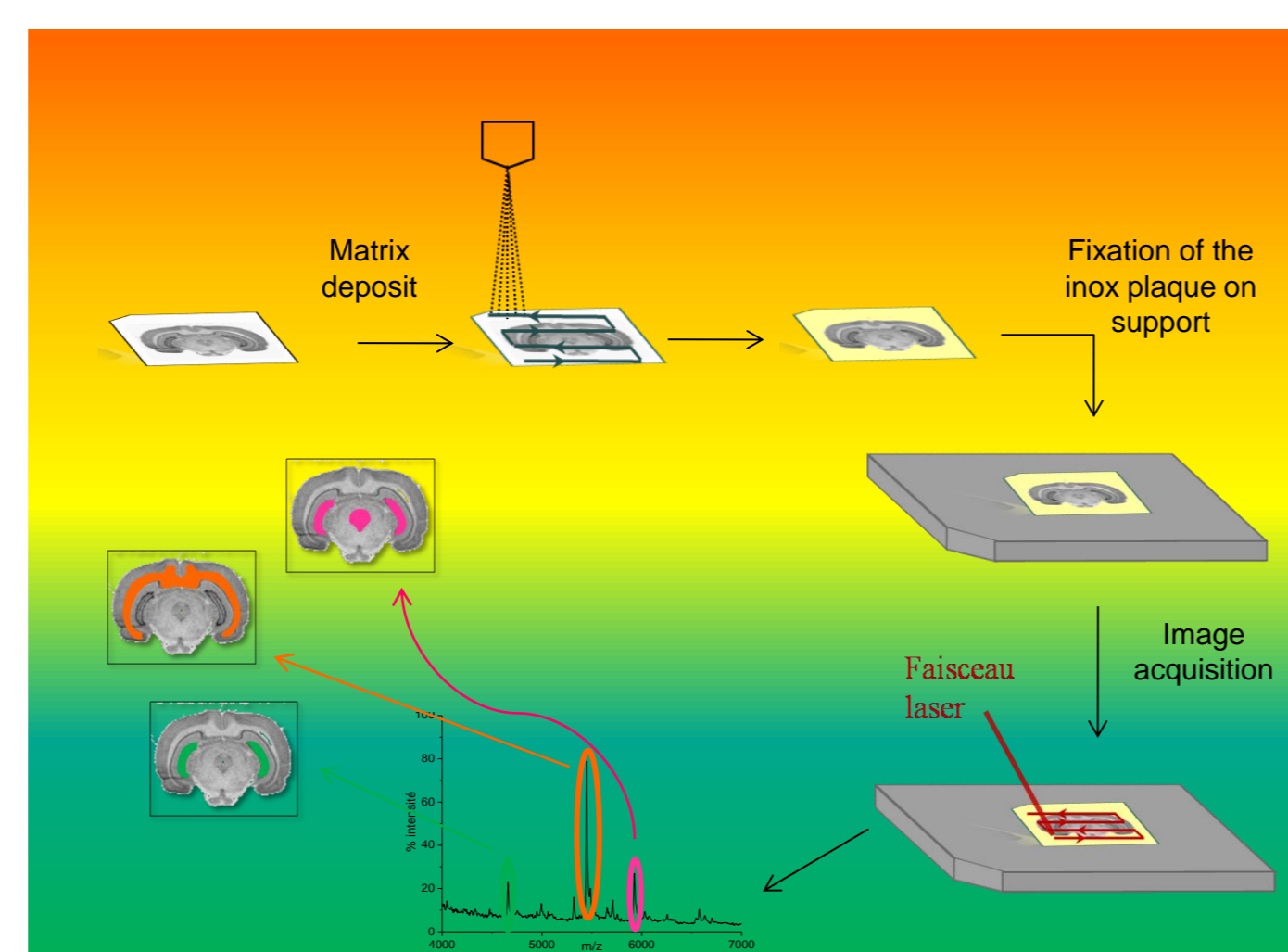
Lipids are the most abundant biomolecules found in the brain, following water, representing up to 50% of its dry weight. These compounds are structural components of cell membranes, and have various functions of precursors, biomessengers, and signal transduction. Marked alterations in their composition have been reported to occur during neurological disorders.

Until now, many studies have been interested in brain lipid content. However, the methods used to identify lipids always involve extraction prior to analysis, which destroys any information relevant to tissue localization. Lipid staining in tissues is possible with fluorescent or classic histological dyes but is not specific. Rare are the specific molecular probes such as immunohistochemical tools able to detect lipids in tissue. Therefore, brain tissue lipidomic imaging is crucial to precise anatomic localization of lipid species in cerebral structures.

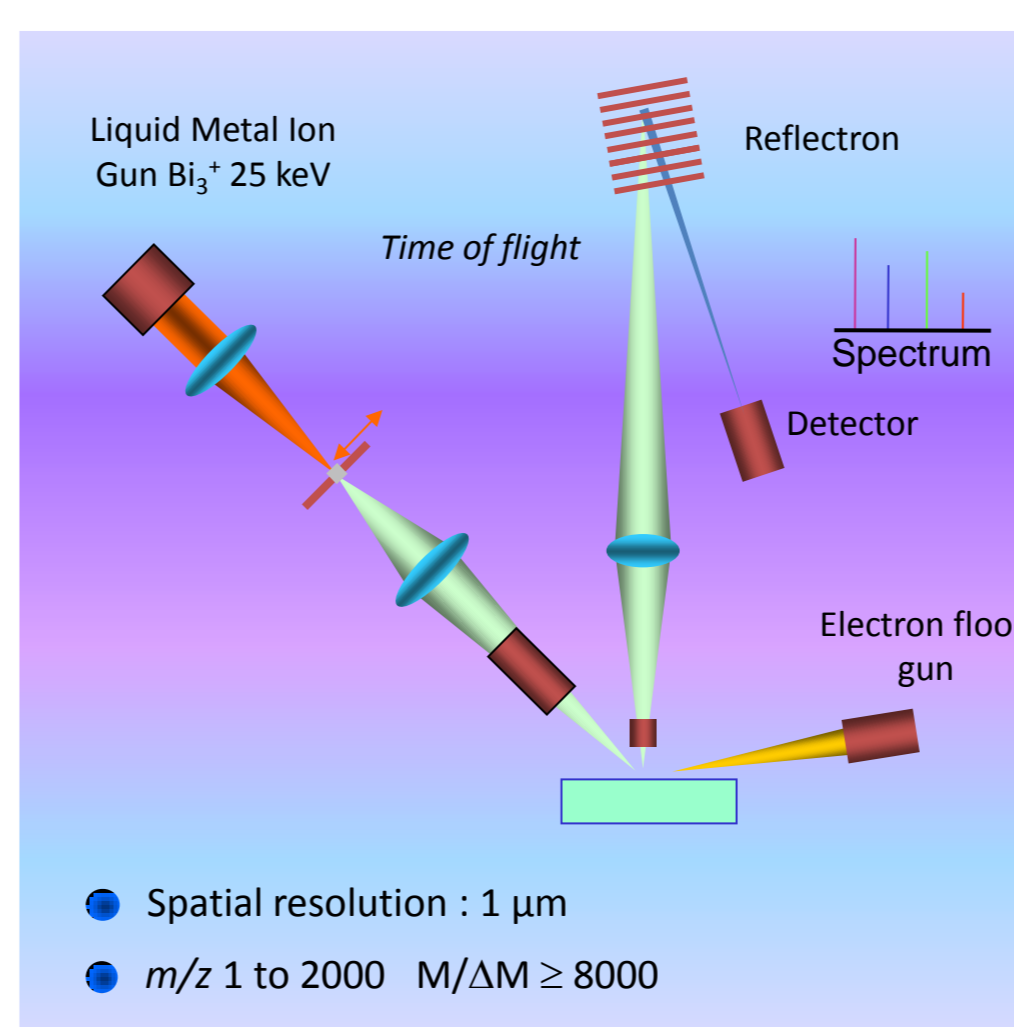
In this study, we used two powerful mass spectrometry imaging methods, MALDI-TOF/TOF¹ (matrix-assisted laser desorption/ionization) and TOF-SIMS² (time-of-flight secondary ion mass spectrometry), in order to detect and localize lipid species in rat brain and human temporal cortex, both at regional and cellular levels. The first method can perform *in situ* structural identifications by MS/MS, while the second is able to localize species with a spatial resolution of less than 1 μm³.

We focused on cholesterol and on the most quantitatively relevant glycerophospholipids (PC, PE, PS, PI) described in literature, their composition greatly altering neural membrane stability, fluidity and permeability. The results showed differential repartition of these lipids in cell bodies or dendrites of grey matter, and in myelinated axons.

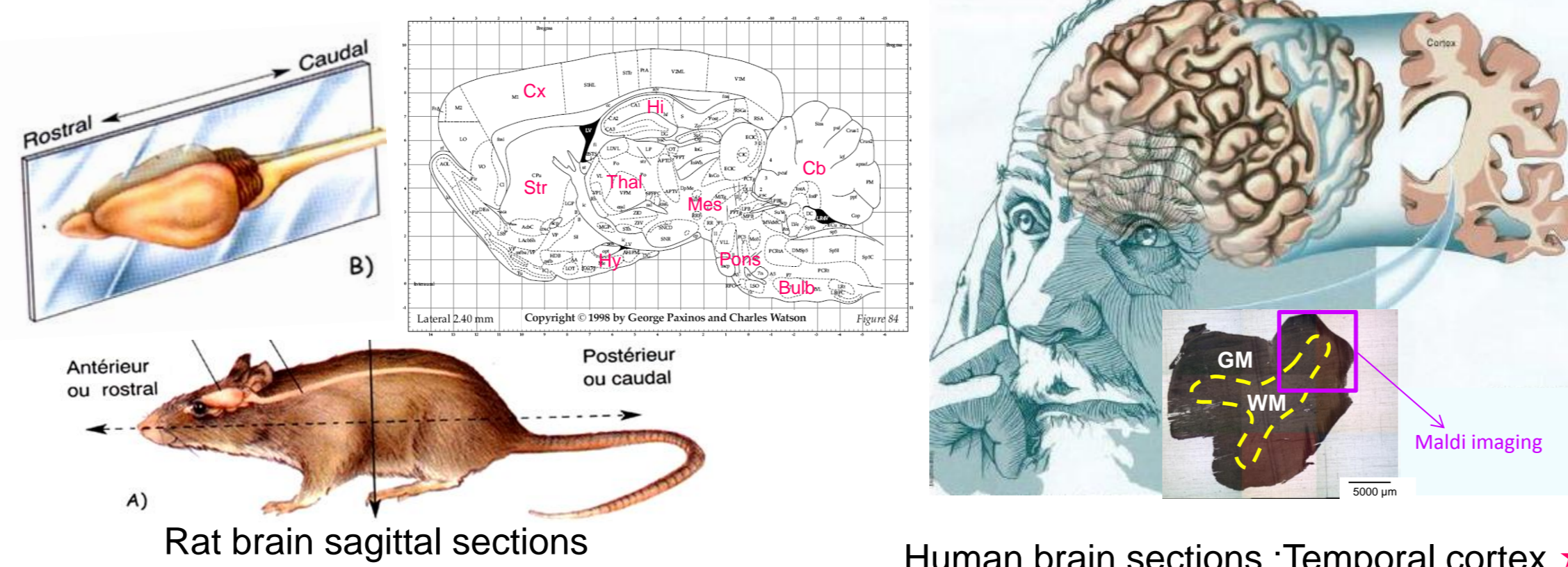
MALDI-TOF/TOF



TOF-SIMS



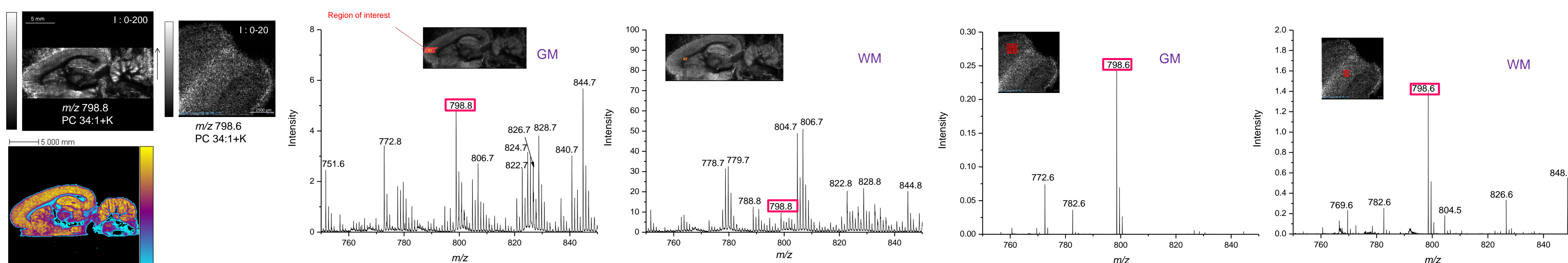
SAMPLES



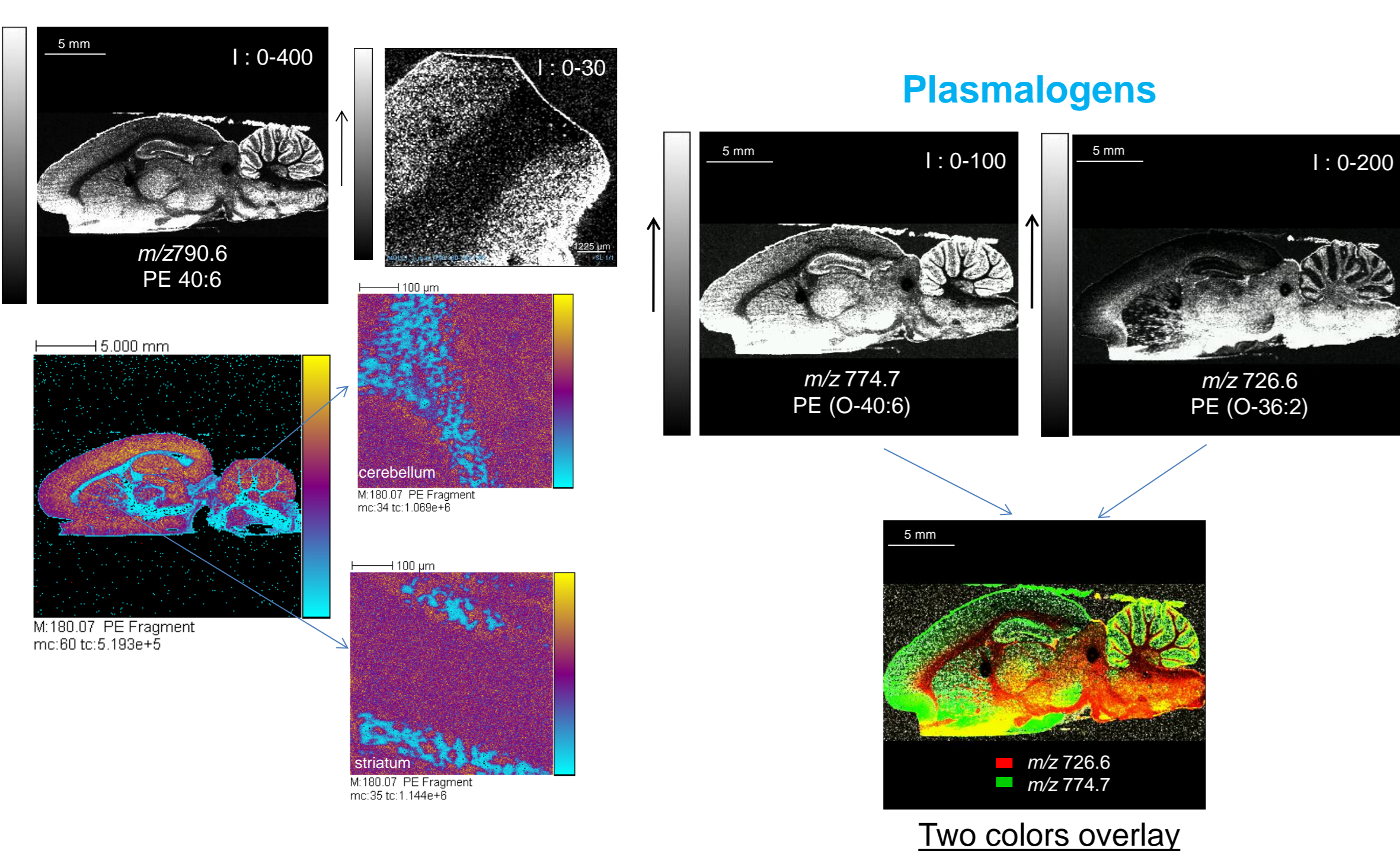
Species	Localization and abundance	Grey Matter (GM)	White Matter (WM)	Structures
Cholesterol [M+H ₂ O] ⁺ m/z 369.35 [M+H] ⁺ m/z 385.35	38±2% of total lipids in rat brain cortex ⁶ 14-16 mg/g brain ww ¹¹		✓	
PC PC 34:1 16:0/22:6 [M+K] ⁺ m/z 798.54	20-23 mg/g brain ww ^{7,8,9,10} 20±1% of total lipids in brain cortex ⁶ 30-40% of PC in cortex (PlsPC 34:0:1-2% of PC) ^{5,6}	✓		
PE PE 40:6 (18:0/22:6) [M+H] ⁺ m/z 790.54 PE O-40:6 (p18:0/22:6) [M+H] ⁺ m/z 774.54 PE O-36:2 (p18:1/18:1) [M+H] ⁺ m/z 726.54	15-20 mg/g brain ww ^{7,8,9,10} 22±2% of total lipids in brain cortex ⁶ 20-35% of PE in cortex ⁶ 10-20% of PE in cortex ^{4,5,6} 8-15% of PE in cortex ^{4,5,6}	✓ ✓		
PS PS 40:6 (18:0/22:6) [M+H] ⁺ m/z 834.53	4-8 mg/g brain ww ^{7,8,9,10} 35-50% of PS in cortex ^{6,6}	✓		
PI PI 38:4 (18:0/20:4) [M+H] ⁺ m/z 885.55	1-2 mg/g brain ww ^{7,8,9,10} 50-70% of PI in cortex ^{5,6}		✓	

Cholesterol represents 40% of total lipids in brain, Glycerophospholipids : 36%, Sphingolipids : 15%, Plasmalogens : 9.5%⁶
Total amount of PL in rat brain = 42±1 mg/g brain, wet weight⁹
PC and PE represent 80% of total glycerophospholipids

PHOSPHATIDYLCHOLINES

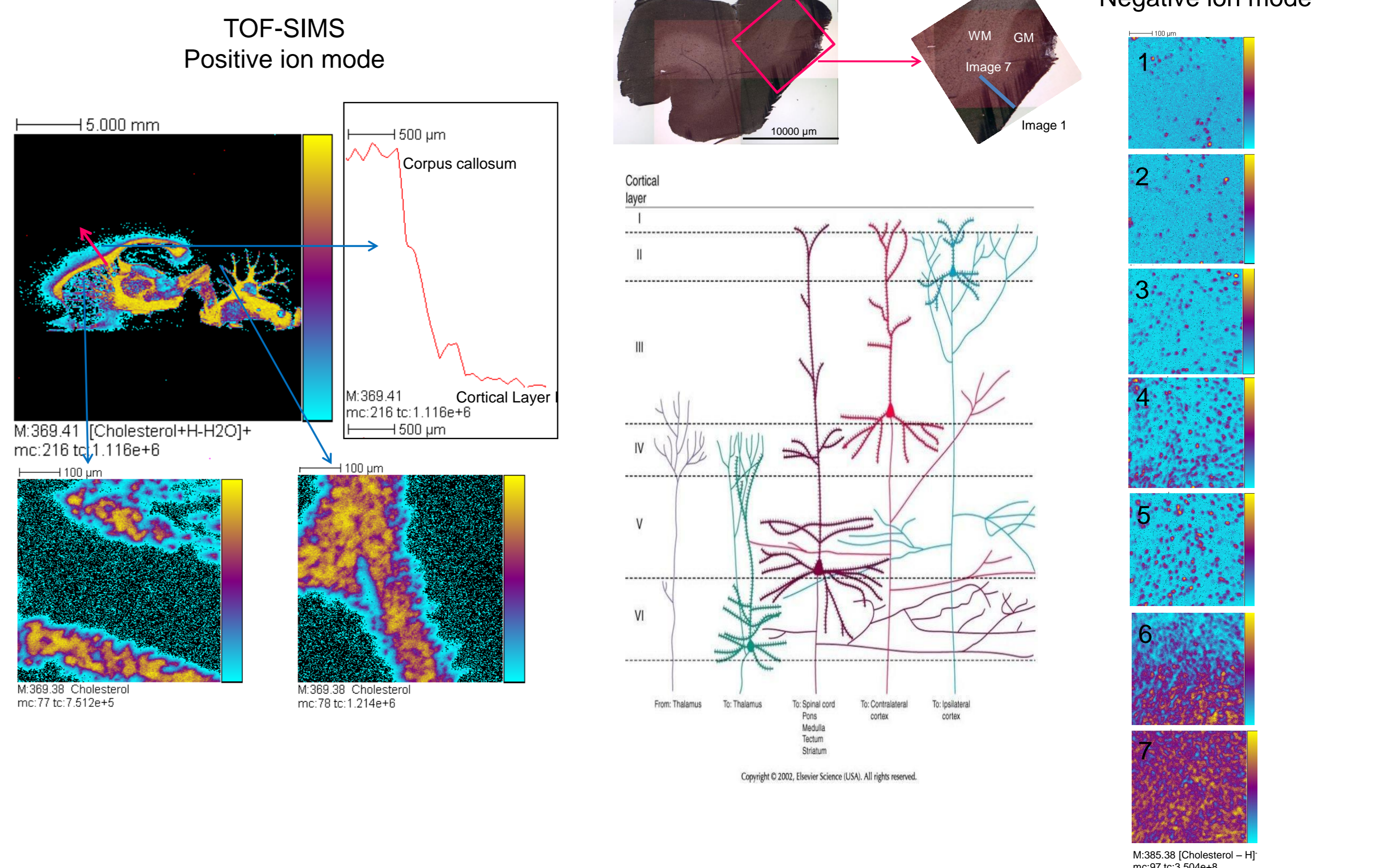


PHOSPHATIDYLETHANOLAMINES

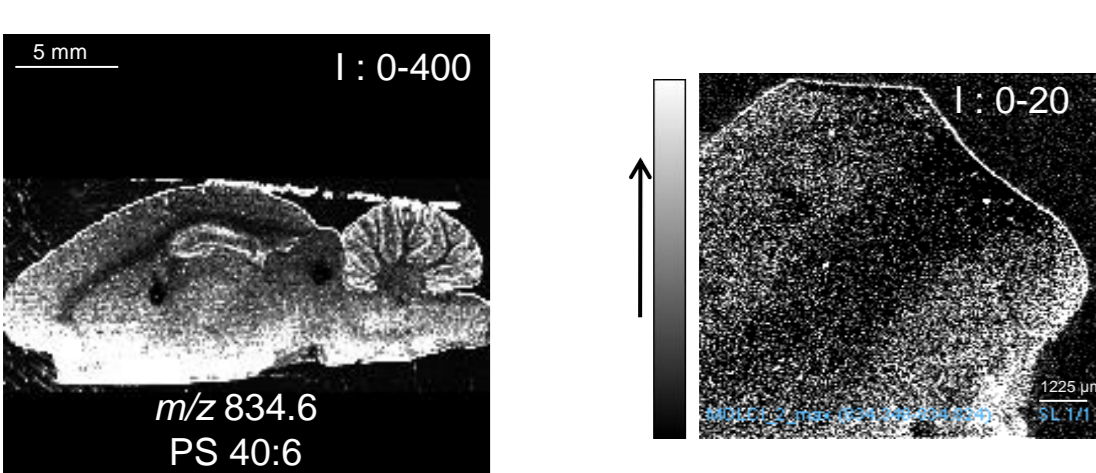


Color scale for TOF-SIMS imaging
mc = maximal number of counts in a pixel
tc = total number of counts for the whole image

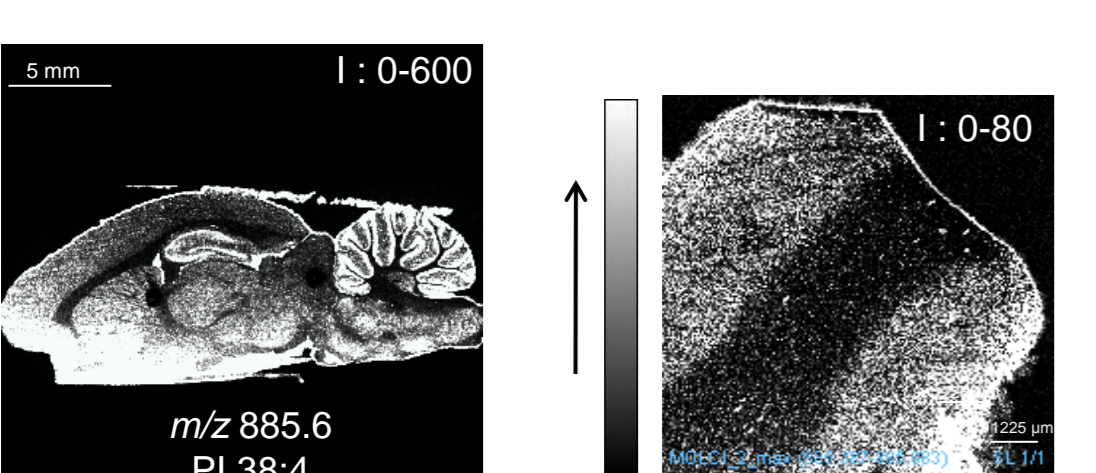
CHOLESTEROL



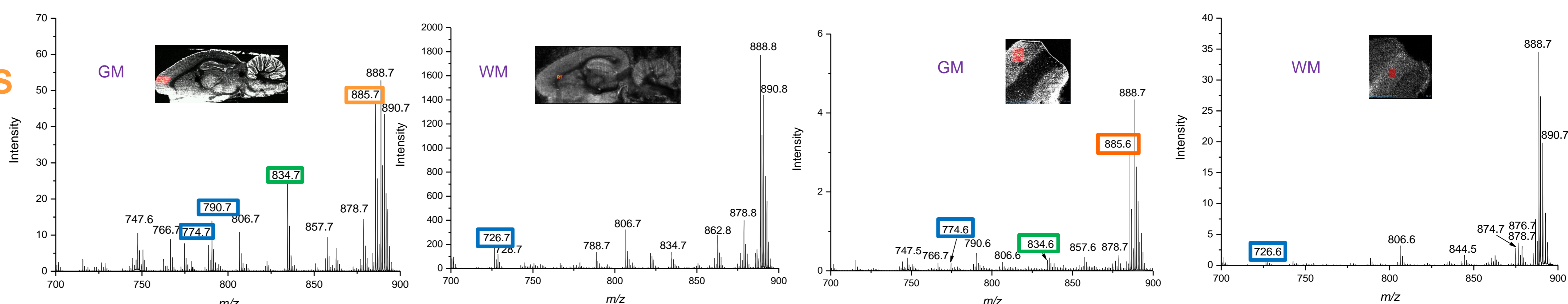
PHOSPHATIDYLSERINES



PHOSPHATIDYLINOSITOLS



MALDI-TOF Negative ion mode



REFERENCES

- Stoeckli M, Chauvrand P, Hallahan D.E., Caprioli R. M. Imaging mass spectrometry: A new technology for the analysis of protein expression in mammalian tissues. *Nat. Med.* 2001, Vol. 7: 493-496.
- Brunelle A, Laprèvote O. Recent Advances in Biological Tissue Imaging with Time-of-Flight Secondary Ion Mass Spectrometry: Polyatomic Ion Sources, Sample Preparation, and Applications. *Curr. Pharm. Design* 2007 Vol. 13: 3335-3343.
- Benabdellah F, Seyer A, Quinon L, Touboul D, Brunelle A, Laprèvote O. Mass spectrometry imaging of rat brain sections: nanomolar sensitivity with MALDI versus nanometer resolution by TOF-SIMS. *Anal. Bioanal. Chem.* 2010 Vol. 396: 151-162.
- Han X, Holtzman D.M., McKel D.W. Plasmalogen deficiency in early Alzheimer's disease subjects and in animal models: molecular characterization using electrospray ionization mass spectrometry. *J. Neurochem.* 2001, Vol. 77: 1168-1180.
- Kikani R, Somersari P, Tytilä J. Analysis of phospholipid molecular species in brains from patients with infantile and juvenile neuronal ceroid lipofuscinosis using liquid chromatography-electrospray ionization mass spectrometry. *J. Neurochem.* 2003, Vol. 84: 1051-1065.
- Little S.J., Lynch M.A., Manku M., Nicolaou A. Docosahexaenoic acid-induced changes in phospholipids in cortex of young and aged rats: A lipidomic analysis. *Prostaglandins, Leukotrienes and Essential Fatty Acids.* 2007 Vol. 77: 155-162.
- Lutzke BS, Braughler JM. An improved method for the identification and quantitation of biological lipids by HPLC using laser light-scattering detection. *J. Lipid Res.* 1990 Vol. 31(11): 2127-2130.
- Metz KS, Dunphy LK. Absolute quantitation of tissue phospholipids using 31P NMR spectroscopy. *J. Neurochem.* 1996 Vol. 67(10): 2251-2265.
- Norris C, Fong B, MacGibbon A, McClarrow P. Analysis of phospholipids in rat brain using liquid chromatography-mass spectrometry. *Lipids.* 2009 Vol. 44(11): 1047-1054.
- Wells MA, Dittmer JC. A comprehensive study of the postnatal changes in the concentration of the lipids of developing rat brain. *Biochemistry.* 1987 Vol. 26(10): 3169-3175.
- Dietschy J.M. and Turley S.D. Cholesterol metabolism in the central nervous system during early development and in the mature animal. *J. Lipid Res.* 2004 Vol. 45: 1375-1397.

* Thanks to Charles Duyckaerts GIE-Neurocib