MASS SPECTROMETRY IMAGING FOR REVEALING METABOLIC PATHWAYS OF A LIVE MOUSE BRAIN

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Introduction

Desorption electrospray ionization mass spectrometry imaging (DESI-MSI) is a powerful tool that allows an untargeted investigation and spatial distribution of molecular species in various tissue samples.[1] In this work, we first investigated the metabolites in mouse brain tissues using DESI-MSI and deciphered the spectra of molecules that affected neurophysiologic and cell signaling life processes. The study provides insights into the relationships between complex brain functions and featured metabolites in the mouse brain. We then applied DESI-MSI to metabolite profiling using disease and healthy tissue samples. To investigate whether metabolites with molecular information and spatial distribution information can be used as disease biomarkers, we began a preliminary study of diabetic mouse heart tissues using DESI-MSI.[2] The metabolites that show different spatial distribution in disease tissues and control tissues also help us to understand the disease mechanism of diabetic heart.

Method and Materials

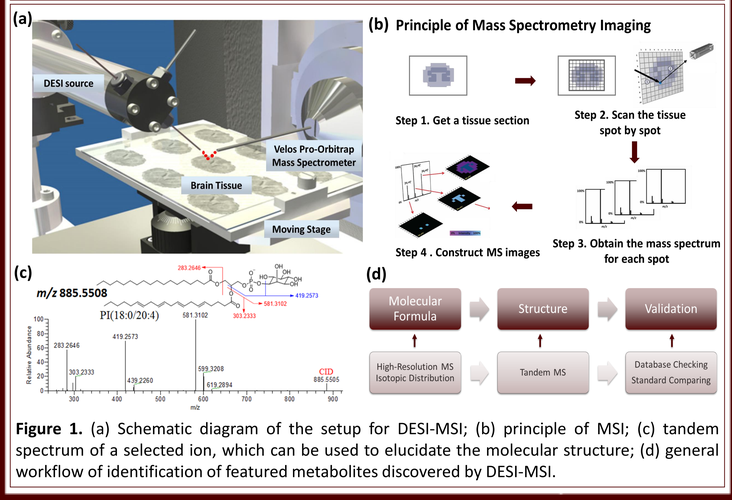

Figure 1. (a) Schematic diagram of the setup for DESI-MSI; (b) principle of MSI; (c) tandem spectrum of a selected ion, which can be used to elucidate the molecular structure; (d) general workflow of identification of featured metabolites discovered by DESI-MSI.

Results and Discussion

Mass spectrometry imaging of mouse brain tissue sections

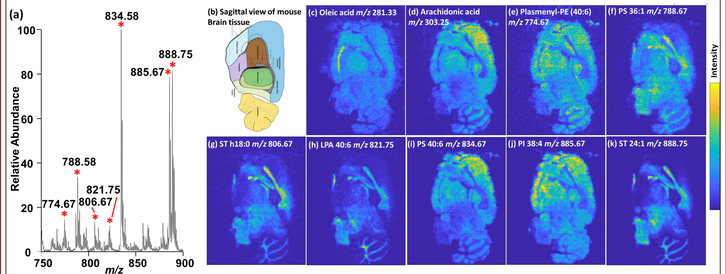

Figure 2. (a) Negative-ion mass spectrum recorded on a mouse brain section during the DESI-MSI experiment; (b) sagittal view of a mouse brain structure; (c)-(k) ion images of oleic acid, arachidonic acid, plasmenyl-PE 40:6, PS 36:1, ST h18:0, LPA 40:6, PI 38:4, ST 24:1.

The lipid distributions in brain tissue section are highly associated with brain functions.[3] For example, the image of lipid at *m/z* 885.67 (PI 38:4) (Fig. 2j), shows a relatively homogeneous distribution across the entire brain tissue section except the lateral ventricle. The distribution of lipid at *m/z* 888.75 (ST 24:1) (Fig. 2k), resembles the distinctive corpus callosum and striatum anatomic structures in the brain section. Moreover, the distribution of lipid ST 24:1 shows complementary localization with lipid PS 40:6 at *m/z* 834.67 (Fig. 2i).

Discovery of featured metabolites in heart tissues sections

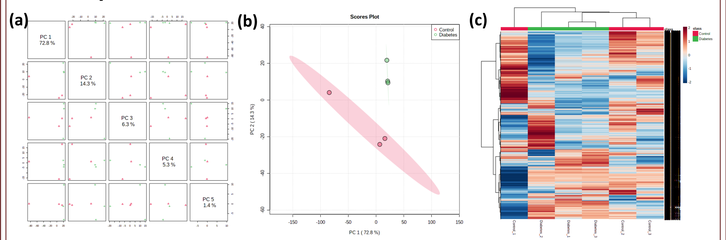

Figure 3. Statistical analysis of MSI data. (a) Pairwise score plots between the selected PCs (b) scores plot between the selected PCs; (c) clustering result shown as heatmap.

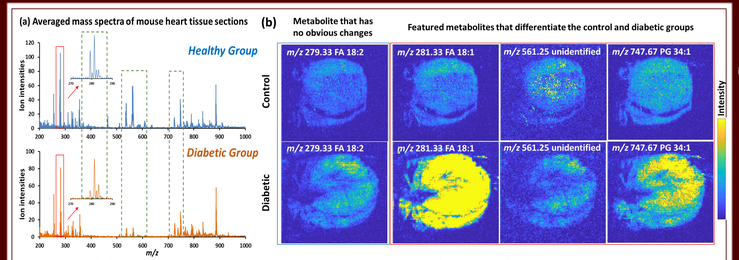

Figure 4. (a) Representative mass spectra with averaged scans of mouse heart tissue sections from healthy and diabetic groups (negative-ion mode); (b) ion images of the metabolites that have no obvious changes and featured metabolites that differentiate the healthy and diabetic groups. The diabetic mice were treated with high fat and high glucose diet for 6 months.

Conclusions

DESI-MSI of healthy mouse brain tissue sections provides the spatial distributions of more than 100 metabolites including lipids of PE, PS, PI, ST, which are associated with the brain structures and biofunctions.

Statistical analysis of metabolic species from mouse diabetic and control groups shows the apparent differences between the two groups. Featured metabolites were identified. Metabolites at m/z 281.33, m/z 561.25 and m/z 747.67 are possibly involved in the metabolic pathways associated with diabetes.

Acknowledgement & Team Members

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References

[1] A. R. Buchberger, K. DeLaney, J. Johnson, L. Li, *Anal. Chem.* **2018**, *90*, 240-265.

[2] S. T. P. Mezger, A. M. A. Mingels, O. Bekers, B. Cillero-Pastor, R. M. A. Heeren, *Anal. Bioanal. Chem.* **2019**, *411*, 3709-3720.

[3] J. M. Wiseman, D. R. Ifa, Q. Song, R. G. Cooks, *Angew. Chem. Int. Ed.* **2006**, *45*, 7188-7192.

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