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Mass Spectrometry for Single Cell Imaging

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Nowadays, it is essential in cellular analysis to visualize cellular populations and pharmaceuticals and disclose information about spatial distribution of biomolecules in a high-throughput mode. To serve this purpose, numerous techniques have been developed. One of them is mass spectrometry imaging (MSI). Its advantage over other technologies such as labeling with radionuclide or fluorescent tags is that it requires no information about biomolecules beforehand. Meanwhile, tons of biomolecules including unknown ones can be detected simultaneously from a single MSI experiment, which allows for direct sub-cellular mapping of biomolecules in a high resolution and high throughput way.

MSI can analyze a wide range of materials and molecules, for which identification, relative quantification, and even absolute quantification can be achieved [1-5]. Typically, there are two classes of mass spectrometry imaging: MALDI-MS (Matrix Assisted Laser Desorption and Ionization Mass Spectrometry) imaging and SIMS (Second Ion Mass Spectrometry) imaging. In MALDI-MS imaging, molecules within a matrix are desorbed from a surface as laser is scanned across the matrix [6] and then detected by a time-of-flight (TOF) mass spectrometer. In SIMS imaging, an accelerated primary ion beam bombards the surface and generates secondary ions [6], which are then analyzed by a time-of-flight (TOF) mass spectrometer in static SIMS imaging or by a magnetic/electrostatic sector mass spectrometer in dynamic SIMS imaging. SIMS imaging provides information about small fragments of a particular biomolecular species or class, e.g., phosphorous ions on the backbone of nucleic acids [7]. It offers the highest spatial resolution (<50nm) but is limited to a relatively narrow mass range. MADLI-MS imaging, on the contrary, is a soft ionization method and applies to a wide mass range. Hence, it is suitable for analysis of intact biomolecules such as proteins, lipids and DNA.

There are challenges faced by MSI analysis. For example, MALDI-MS imaging is restricted in terms of spatial resolution. SIMS imaging, on the other hand, can routinely reach spatial resolutions at the submicron level [8], but it is subject to narrow mass range [9]. There have also been progresses made to meet and tackle these challenges. For MALDI-MS imaging, one way of improving spatial resolution is through more advanced techniques of sample preparation. These techniques include MALDI matrix sublimation, which can help obtain more uniform microcrystals in matrix application and sample expansion by thaw-mounting the sample to be analyzed on a stretchable material, which physically enlarges sample area prior to matrix application [10,11]. Spatial resolution of MALDI-MS imaging can also be improved by optimizing laser beam to either reduce the spot size or utilize overlapped laser spot [12,13]. For SIMS imaging, its mass range has been recently extended to around 2 kDa [14] by the use of cluster ion sources (e.g., C_{60}^+ and Bi_3^+). Moreover, matrix enhancement has also been utilized to extend the mass range considerably [15].

Besides MALDI-MS and SIMS, other mass spectrometry methods can also serve as potential imaging techniques with high sensitivity and quantitative analysis platform. They include the inductively coupled plasma (ICP) MS [16], scanning near-field optical microscopy (SNOM) MS [17], and nanostructure-initiator mass spectrometry (NIMS) [18]. With all these powerful techniques, it is expected that mass spectrometry imaging will continue to play an essential role in single cell imaging and cellular analysis in general.

References

1. Chandra S, Tjarks W, Lorey DR, Barth RF (2008) Quantitative subcellular imaging of boron compounds in individual mitotic and interphase human glioblastoma cells with imaging secondary ion mass spectrometry (SIMS). J Microsc 229: 92-103.
2. Smith DR, Chandra S, Barth RF, Yang W, Joel DD, et al. (2001) Quantitative imaging and microlocalization of boron-10 in brain tumors and infiltrating tumor cells by SIMS ion microscopy: relevance to neutron capture therapy. Cancer Res 61: 8179-8187.
3. Ausserer WA, Ling YC, Chandra S, Morrison GH (1989) Quantitative imaging of boron, calcium, magnesium, potassium, and sodium distributions in cultured cells with ion microscopy. Anal Chem 61: 2690-2695.
4. Rubakhin SS, Sweedler JV (2008) Quantitative measurements of cell-cell signaling peptides with single-cell MALDI MS. Anal Chem 80: 7128-7136.
5. Chen R, Li L (2010) Mass spectral imaging and profiling of neuropeptides at the organ and cellular domains. Anal Bioanal Chem 397: 3185-3193.
6. Boxer SG, Kraft ML, Weber PK (2009) Advances in imaging secondary ion mass spectrometry for biological samples. Annu Rev Biophys 38: 53-74.
7. Wedlock LE, Kilburn MR, Cliff JB, Filgueira L, Saunders M, et al. (2011) Visualising gold inside tumour cells following treatment with an antitumour gold (I) complex. Metallomics 3: 917-925.
8. Lanni EJ, Rubakhin SS, Sweedler JV (2012) Mass spectrometry imaging and profiling of single cells. J Proteomics 75: 5036-51.
9. Schober Y, Guenther S, Spengler B, Römpp A (2012) Single cell matrix-assisted laser desorption ionization mass spectrometry imaging. Anal Chem 84: 6293-6297.
10. Monroe EB, Jurchen JC, Koszczuk BA, Losh JL, Rubakhin SS, et al. (2006) Massively parallel sample preparation for the MALDI MS analyses of tissues. Anal Chem 78: 6826-6832.
11. Tucker KR, Lanni EJ, Serebryannyy LA, Rubakhin SS, Sweedler JV (2011) Stretched tissue mounting for MALDI mass spectrometry imaging. Anal Chem 83: 9181-9185.
12. Zavalin A, Todd EM, Rawhouser PD, Yang J, Norris JL, et al. (2012) Direct imaging of single cells and tissue at sub-cellular spatial resolution using transmission geometry MALDI MS. J Mass Spectrom 47.
13. Jurchen JC, Rubakhin SS, Sweedler JV (2005) MALDI-MS imaging of features smaller than the size of the laser beam. J Am Soc Mass Spectrom 16: 1654-1659.
14. Komatsu M, Murayama Y, Hashimoto H (2008) Protein fragment imaging using ink jet printing digestion technique. Appl Surf Sci 255: 1162-1164.
15. Altelaar AFM, van Minnen J, Jimenez CR, Heeren RM, Piersma SR (2005)

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Direct molecular imaging of *Lymnaea stagnalis* nervous tissue at subcellular spatial resolution by mass spectrometry. Anal Chem 77: 735-741.

16. Zoriy MV, Becker JS (2009) Near-field laser ablation inductively coupled plasma mass spectrometry: a novel elemental analytical technique at the nanometer scale. Rapid Commun Mass Spectrom 23: 23-30.

17. Stöckle R, Setz P, Deckert V, Lippert T, Wokaun A, et al. (2001) Nanoscale atmospheric pressure laser ablation-mass spectrometry. Anal Chem 73: 1399-1402.

18. Greving MP, Patti GJ, Siuzdak G (2011) Nanostructure-initiator mass spectrometry metabolite analysis and imaging. Anal Chem 83: 2-7.