MALDI-MSI: from developments to applications

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Elucidating changes at the proteome level for better understanding of cell signalisation pathways modifications in abnormal cells is a complex task that requires the development and use of dedicated and new tools. In this respect, MALDI Imaging has shown growing interest for proteomics applications in biology and clinical fields by allowing pathological biomarkers to be discovered and their distribution to be followed directly from tumour tissues. On tissue proteomics is a highly interesting approach for biomarkers hunting and has shown to avoid several of the problems classically encountered with fluids proteomic. However, even if the continuously growing number of publications of MALDI imaging applications to pathologies, methodology strategies still require to be improved.

A first part of developments concern MALDI imaging of Formalin-Fixed and Paraffin-Embedded (FFPE) Tissues[1]. In fact, the biggest part of hospital tissue banks consists of FFPE blocks. Such samples are highly advantageous for pathologists since they do present a great stability in time. Although, such samples are a priori not well adapted for MALDI experiments. We have studied new methodological strategies for retrieving information and imaging old FFPE samples. *In situ* controlled enzymatic digestion of tissues has proved to be the easiest solution to image and get structural information on peptides and proteins from FFPE samples.

In situ chemical derivatization of peptides obtained after enzymatic digestions were also studied. Derivatizations have shown to be very helpful for peptides/proteins identification by either allowing de novo sequencing or leading to high increase in identification score after databanks interrogation.

On the other hand, we have also developed a new concept for both using MALDI imaging as a validation tool in clinical researches as well as broadening the range of analysable molecules by MALDI imaging to mRNA, higher mass proteins or sugars. This so-called specific imaging[2] is a targeted methodology for specifically tracking a probe of interest. We have developed new types of reporters adapted to MS detection that can be combined with different types of probes such as antibodies, oligonucleotides or lectin probes by constructing reporters including photoceavable moieties. By combining our specifically tagged probes with different hybridization techniques such as ISH or IHC, we can now image antigens, mRNA and glycoprotein's by imaging peptide reporter released during MALDI experiments by photocleavage under the laser irradiation. This makes MALDI Imaging becoming an interesting tool for biomarkers validation with possible correlation at the transcriptome/proteome level.

These developments were used in several applications including ovarian cancer[3] and animal models for Parkinson[4] for biomarkers hunting and validation. This proves that MALDI imaging has now found is way to be considered as an efficient tool for pathological proteomics.

Keywords: Imaging of FFPE tissues, *In situ* structural elucidation, Imaging of mRNA, Imaging antigens, Imaging of saccharides

References

[**1**] Lemaire R., Desmons A., Day R., Salzet M., Fournier I. (**2007**) Direct analysis and MALDI imaging on formalin fixed paraffin embedded tissue sections (FFPE). *J. Proteome Res. 6*(4): 1295-305

[**2**] Lemaire R., Stauber J., Wisztorski M., Van Camp C., Desmons A., Deschamps M., Proess G., Rudlof I., Woods A. S., Day R., Salzet M., Fournier I. (**2007**) Tag-Mass: Specific Molecular Imaging of Transcriptome and Proteome by Mass Spectrometry Based on Photocleavable Tag, *J. Proteome Res.* 6(6):2057-67.

[**3**] R. Lemaire, S. Aït-Menguellet, J. Stauber, J-P. Lucot, P. Collinet, M-O. Farine, D. Vinatier, R. Day, P. Ducoroy, M. Salzet, I. Fournier, (**2007**) Biomarker Discovery and Validation by Profiling and Specific Imaging by Mass Spectrometry: Reg-Alpha Fragment is a Biomarker of Ovary Cancer. *J. Proteome Res. 6*(11): 4127-34

[**4**] Stauber, J., Lemaire R., J. Franck, D. Bonnel, Day R., Fournier I., Salzet M. (**2008**) Molecular Profiling of Experimental Parkinson's disease: Direct Analysis of Peptides and Proteins in Formalin Fixed and Paraffin Embedded Rat Brain Tissue Sections by MALDI Mass Spectrometry. *J. Proteome Res. 7*(3): 969-978