Challenges of protein PTM analysis by mass spectrometry

Giovanni Chiappetta, Massamba Ndiaye, Shakir Shakir, Joelle Vinh

Biological Mass Spectrometry and Proteomics SMBP CNRS USR3149 ESPCI Paris, PSL Research University. Email: joelle.vinh@espci.fr

Joëlle Vinh is specialized in analytical chemistry and biological mass spectrometry. She is presently the head of the Biological Mass Spectrometry and Proteomics laboratory at ESPCI Paris, PSL Research University. After a postdoctoral position in proteomics as an HFSP fellowship for 2 years at the Southern Denmark University in Protein Research group headed with Pr.Peter Roepstorff and Pr. Ole Jensen, she joined the Neurobiology and Cellular Diversity laboratory (ESPCI Paris) in 2000 as a CNRS research scientist. She set up the ESPCI biological mass spectrometry facility, with a first national recognition in 2001 from the National French Network (RIO, CNRS, Inserm, INRA and CEA). She worked as group leader of the biological mass spectrometry group since 2002, coordinating the RIO platform for proteomics at ESPCI. She co-authored more than 80 publications in international journals all involving biological mass spectrometry implementation. Working on the characterization of proteins (identification, post-translational modifications study, sequencing) using the MS proteomics toolbox, she focused more specifically on nano separations coupling with mass spectrometry for multidimensional analyses. Joelle Vinh coordinated the Network Analytics in Ile de France and is director of the CNRS Group of Scientific Interest for Analytical Sciences. She is member of the steering committee of Labex Institut Pierre Gilles de Gennes for microfluidics

Abstract:

Very rapid technological developments in separative sciences and mass spectrometry have made it possible to always better characterize proteins in biological models. The proteoforms are the final products of genes, and result from alternative RNA splicing (transcriptome) and from maturation of protein isoforms (proteome) associated to covalent post-translational modifications (PTMs). They interact with the molecular environment (proteins, ligands, oligonucleotides) and regulate many cellular processes. Their function, location, stability is often dynamically altered by PTMs. A protein can be declined into several proteoforms with multiple functions. PTM's characterization is therefore essential to understand and act on living organisms.

There are many PTMs (more than 1000 were listed in Uniprot in 2017). In order to finely characterize these changes, proteomic approaches in mass spectrometry are gradually developing with specific strategies to take into account their great molecular diversity. In order to better describe the underlying biological phenomena, it is necessary to identify and locate them and then quantify the proportion of proteoforms that are present. The control of many biological processes can result from the regulation of very low abundant and labile species. Diverse analytical strate-

gies for the characterization of these species were proposed, ranging from sample preparation to data processing, but still based on mass spectrometry analysis for the quantification and the structural characterization of multiple PTMs. Here we will present the evolution of some of these strategies, their similarities and differences, and the challenges and limitations associated with them, illustrating in particular this approach on the analysis of redox PTMs.