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Issues and solutions for the quantification of post-translational or induced protein modifications

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The accurate quantification of biological processes is one of the new frontiers of systems biology and hypothesis-driven investigations. Quantification methods have been developed with the aim to measure the abundance of the protein itself. So far, the quantification of modifications, whether post-translational or chemically induced *in vivo* or *in vitro*, has been dealt with as an extension of protein level measurements. As a consequence, experimental setups and interpretation algorithms are ill-designed to measure the extent of modification at one or more amino-acid position(s).

Here we argue that ad-hoc methods need to be developed to deal with the issues that are specific to modification quantification. Focusing on methods based on proteolysis of the target protein prior to mass spectrometry analysis, some of the issues and methods pre-requirements can be identified:

The modification can change the solubility and the degree of ionization of peptides containing the modified residues, so that the method should not be sensitive to these effects. If the modifiable residues are part of the cleavage specificity spectrum of the proteinase, missed cleavages can appear, so that this particular proteinase should be avoided, or missed cleavages dealt with. The developed tools should allow for the straightforward visualization of the result and if possible, integrate with popular protein quantification tools such as Skyline.

We have developed two complementary approaches to start dealing with these issues. The experimental setups, computation of modification ratio at each target residue, and a graphical representation of the result will be presented.

Biography

Martine Cadene has PhD and a Doctorate in Pharmacy from Université Louis Pasteur of Strasbourg, France, and a Habilitation à Diriger des Recherches from Université d'Orléans, France. Following Post-doctoral and Research Associate positions with Ron Beavis (NYU) and Brian Chait (Rockefeller University, New York), in 2005 she became a CNRS group leader at CBM Orléans, France. She has published ~34 papers including several Nature articles with Nobel Prize winner Rod MacKinnon.

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