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INTRODUCTION

Special issue on protein species

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The great efforts of the last 20 years resulted in a highly automated and sensitive proteomics technology at the protein level with sensitive detection of posttranslational modifications on peptides. The protein expression concept was an important motor for this development. The next step in proteomics is to reach the protein species level to obtain access to the functional active molecules. Together with the amino acid sequence, the combination of the posttranslational modifications decides for the function. If we want to understand function at the molecular level, we have to learn to work with the protein species concept, which is introduced in the Editorial of the Special Issue Protein Species (Jungblut and Schlüter 2011). This Special Issue is a first attempt to show the state of the art of this concept.

There are several hundred known posttranslational modifications and because it is not possible here to consider all of them, a focus had to be set to phosphorylation (Wisniewski 2011), glucosylation (Sisu et al. 2011; Wisniewski 2011), ADP ribosylation (Laing et al. 2011), and proteases (Klein and Bischoff 2011) within four reviews. In another review, Meyer et al. (2011), the challenges to obtain 100% sequence coverage, a prerequisite to work at the protein species level, are worked out.

Four articles present technological improvements to obtain access to posttranslational modifications or even protein species. Metal ion-mobilizing additives were suggested to improve the sensitivity of phosphopeptide detection (Seidler et al. 2011). An optimized scoring for different charge states and cleavage improved the identification of *O*-linked glycopeptides from ETD data (Darula et al. 2011). Hoehenwarter et al. (2011) applied linear mathematics for functional analysis of proteins and protein species using shotgun proteomics. In-capillary proteolytic digestion was applied for direct analysis of alpha- and beta-chains of hemoglobins from mammalian blood samples by nano-ESI mass spectrometry (Henning et al. 2011).

In six biological applications protein speciation was observed and it becomes obvious that it is necessary to improve protein–chemical methods to reach the protein species level. An apoptosis-associated oxidation of cysteine and phosphorylation of a proteasomal protein (Schmidt et al. 2011) shows a direct connection between protein species and function. Many posttranslational modifications, amino acid changes, and alternative splice variants were found in a study of microtubule-associated proteins and their interacting partners from mammalian brain (Kozielski et al. 2011). Signatures for human breast cancer were detected already at the posttranslational modification level in histones (Cuomo et al. 2011). 2-DE/MS approaches clearly detected protein speciation in murine heart (Schwab et al. 2011), papillary thyroid carcinomas (Zeindl-Eberhart et al. 2011) and in monocytes of chronic kidney disease patients (Scholze et al. 2011).

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