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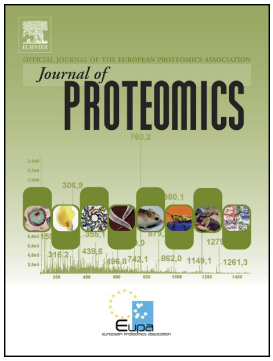

Top-down proteomics: Where we are, where we are going?

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Top-down proteomics: where we are, where we are going?

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Increasing Momentum

After some years spent increasing metrics of proteome coverage, the field of proteomics has increasingly focused on the *quality* of information generated during interrogation of living systems. Another aspect trending presently is to integrate proteomics with data from other "-omics" in order to gain deeper insights into cellular and disease biology. From this perspective, it is apparent that the analysis of intact proteoforms, or top-down proteomics,[1] presents additional advantages. In providing precise compositional information, TDP can add molecular details lost when proteoforms are dissected into proteolytic peptides used in bottom-up proteomics. Although BUP can identify and localize post-translational modifications (PTMs) on proteins, the well-known 'protein inference problem' greatly complicates the elucidation of their global patterns or cross-talk, aspects which can be captured using TDP. This is exemplified by the so-called "histone code", where PTMs comprise combinatorial and highly dynamic patterns resulting from concerted interactions between prior PTMs and histone-modifying enzymes. These patterns govern the reading of histone marks and myriad biomolecular activities, and can be comprehensively described at the proteoform level to help assign the functions of PTM patterns.

It is true that top-down proteomics is technologically challenging, yet perceptions about this are often historical and not updated quickly in the minds of experts or those far