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Top-down and bottom-up two-dimensional mass spectrometry for protein structural characterisation

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Two-dimensional mass spectrometry (2DMS) is a method for tandem mass spectrometry that relies on ion radius modulation instead of ion isolation to correlate between precursor and fragment ion peaks. 2D mass spectra show all the fragmentation patterns of the analytes in a sample. Signal multiplexing yields high signal-to-noise ratios and therefore complete sequence coverage (e.g., for biomolecules) [1]. Modifications can easily be assigned and located visually with precursor ion scans and dissociation lines. Previous studies have established the potential of 2D MS with electron capture dissociation (ECD) for bottom-up proteomics and for the label-free relative quantification for the top-down analysis of biomolecules [2,3]. Covalent labelling methods such as acetylation and oxidative foot-printing can be used to probe the three-dimensional structures of biomolecules, e.g., to study protein-ligand interactions [4,5]. In this study, we combine 2D MS and covalent labelling of proteins for both bottom-up and top-down analysis. We compare the performance of 2D MS vs. LC-MS/MS for the identification, location, and quantification for protein structural characterisation.

References

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