Trapped Ion Chemistry for Rapid Protein Identification

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We are pursuing a strategy for the rapid detection and identification of proteins in mixtures. It is currently directed at the identification of bio-toxins, viruses, and pathogenic bacteria, although a number of other bioanalytical applications might also benefit from this strategy. The approach employs electrospray ionization and quadrupole ion trap tandem mass spectrometry. Electrospray is used because the strategy benefits from the multiple charging phenomenon associated with electrospray. An ion trap is used because it constitutes a flexible platform for MS/MS that can used either on a bench-top or in the field. In contrast with conventional means for the identification of proteins, this approach does not rely on enzymatic digestion. Furthermore, two-dimensional get electrophoresis is not used to separate proteins prior to analysis. Rather, relatively crude protein separations are to be used on-line to provide a limited set of proteins for analysis. Collisional dissociation of targeted proteins is used to identify the protein either via matching to an MS/MS spectral library or to a protein data-base.

Heavy reliance is placed on gas-phase ion chemistry to obviate the use of gel electrophoresis and protein digestion. Both unimolecular dissociation and ion/ion proton transfer reactions are necessary for the overall approach to succeed. Complex mass spectra resulting from mixtures of multiply-charged ions can be simplified by the use of ion/ion proton transfer reactions to yield spectra of largely singly-charged ions. This procedure can simplify significantly the identification of candidate targeted proteins. Dissociation of one or more of the highly-charged ions of the protein in question can then yield a product ion spectrum that might be matched with an MS/MS library spectrum directly. This approach is expected to be effective when a spectrum of the candidate protein is present in the MS/MS library. Alternatively, the product ion spectrum can be reduced to singly-charged ions via ion/ion chemistry so that the spectrum can be interpreted without ambiguity arising from uncertainty in product ion charge state. If there are fragments from a contiguous stretch of amino acids, a sequence tag can be derived from the product ion spectra and used to search a protein data-base. Given that protein data-bases are always likely to be much larger than any MS/MS library, the latter approach is far more likely to be able to identify unanticipated proteins.

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