Secretopeptidomics for the Discovery of Bioactive Peptides

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Current proteomics technologies do not cover naturally occurring peptides, or small molecular weight (less than 10,000 Da) proteins. Given this issue, peptidomics has been advocated to profile these endogenous peptides including biologically active peptides. Unlike proteomics technologies, peptidomics needs to isolate a peptide-rich fraction, which accounts for less than 0.1% of the total net weight of proteins in biological samples. In addition, peptidomics dispenses with enzymatic digestion to keep intact the primary structure of an endogenous peptide. This is important because these peptides often harbor basic amino acid residues targeted by proteases such as trypsin routinely used in proteomics. Practically, a complex mixture of peptides are separated by high-performance liquid chromatography into multiple fractions before tandem mass spectrometric identification. Peptidomics primarily concerns the discovery of novel bioactive peptides; however, this remains a daunting task in view of the high complexity and broad dynamic range of the mammalian peptidome, or all the endogenous peptides present in a given biological system. To overcome this analytical issue, we have focused on culture supernatant from mammalian cells maintained in serum-free condition. We found that in a very specific system almost all the peptides identified were from precursor proteins of a secretory nature, least contaminated by non-specific peptide fragments from cytosolic abundant proteins. We are now made aware that this “pure” peptidome is quite informative for peptide research including the discovery of potential bioactive peptides.