PROTEOMICS: WEIGHING THE EVIDENCE

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There are an estimated 1,000,000 proteins coded by the genes of the human genome. This staggering number coupled to the inherent variety of activities afforded by post-translational modifications and several potential interactions make the whole world of genomics look simple in comparison to the goals of proteomics. Not only is the proteome more diverse, but it is also dynamic in contrast to the static genetic constitution of a given organism. This is expressed not only in the temporal regulation of protein function but also in the modulation of spatial distribution. In other words, a single gene could give rise to a variety of functional proteins each of which may be expressed at different levels at different times and in different sub-cellular sites. To make matters more challenging, proteins often act as part of large complexes. Among these dynamic assemblies are multi-subunit molecular machines which are products of billions of years of evolution. These machines often prove to be elusive targets for most biochemical and biophysical scrutiny. In part this is because these multi-subunit assemblies are not practical to over-express hence most studies depend on isolation of materials from natural sources. Furthermore, many of these macromolecular complexes tend to asymmetric making them less straightforward to study by techniques that profit from data averaging such as NMR and crystallography.

A major boost in the advance of proteomics is the application of mass spectrometry that was made possible by the development of soft ionization methods namely Matrix-assisted Laser desorption (MALDI) and electrospray ionization (ESI). Nano-electrospray conditions provide optimal sensitivity for individual proteins and their peptidic fragments. Electrospray used in this way coupled to tandem mass spectrometry approaches to analyse peptide fragments formed the backbone of most efforts in proteomics worldwide. In parallel to developments in proteomics, mass spectrometry also evolved as an important tool for looking at intact biopolymers. Non-covalent complexes were possible to maintain inside the spectrometer by manipulating solution conditions. Taken together, these advances have allowed mass spectrometry to identify important biological interactors and analyze the largest of complexes.

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