

Progress in Proteomics: What's Working and What's Not

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In the last decade, proteomics has evolved into a major field of biomedical/biological research, but one that has only barely begun to realize its full potential. It arose as the result of a major paradigm shift in the study of proteins and is rooted in the determination of the human genome sequence (and a rapidly growing number of additional genome sequences) and three principal technological advances – 2D gels, protein and nucleic acid arrays and MALDI/ESI mass spectrometry, the last of which has become the dominant driving force. Proteomics has, as its generalized objective, the complete description of individual proteomes, whether they are derived from whole organisms, tissues or other biologically defined subsets. This requires the identification of the structure/function of all proteins in the set including, where present, splice variants and post-translational modifications (PTMs). It also requires the determination of both the stable and transient protein-protein interactions that make up the highly complex cellular networks of even the simplest organisms and, finally, a description of the expression and location of each protein. Not surprisingly, progress in these different areas has been variable. For, example, analyses involving the determination of PTMs in complex samples have been particularly successful, mainly due to advances in mass spectrometry, as illustrated by the determination of O-N-acetylglucosaminylation and its relationship to protein phosphorylation, key modifications in signal transduction pathways. On the other hand, studies meant to identify clinically relevant proteins/peptides (biomarkers) have lagged significantly and, on the whole, have been quite disappointing. This slow progress may be due in part to wrong approaches and in part because new technology (to bring about the next paradigm shift) is needed. Both examples will be discussed with illustrations.

One area of biology that is likely to profit greatly from proteomic research in the near future is the characterization of stem cells (of different origins). Although the medical benefits of human stem cells have probably been as severely overhyped as proteomic technology itself, it is clear that a more extensive wedding of these two potentially highly beneficial areas of biological research could prove to be the mother lode of ‘translational medicine’. A few speculations of what may emerge from stem cell proteomics in the next few years will be presented. Supported in part by USPHS, NIH, National Center for Research Resources Grant RR 01614