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PROTEOMICS: PROGRESS, PROBLEMS, AND POTENTIAL PAYOFFS

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Over the last several years, proteomics has evolved into a major field of biomedical/biological research, but one that is still well short of achieving its vast potential. Arising from a true paradigm shift, it 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. It 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. It also requires the determination of the both the stable and transient protein-protein interactions that make up the highly complex cellular networks of even the simplest organisms. Finally, a description of the expression and location of each protein as well as an implied correlation with both transcriptomic and metabolomic data, determined under the same conditions (or perturbations), is needed. While there have been notable advances in these efforts, which have provide some useful new insights into biology, in general, and human pathology, in particular, there have also been some major disappointments and the efforts to date are, relative to the scope of what remains to be done, still largely superficial. The 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. The progress, problems and potential payoffs are well illustrated by the (largely unsuccessful) search for biomarkers of human disease and by the characterization of mouse and human stem cells, as will be described. Supported in part by USPHS, NIH, National Center for Research Resources Grant RR 01614