[S4-2] *[4/21/2000 (Fri) 14:10~14:50/Room B112, B1 Floor, Bldg 26]*

Proteome technology and its application to the study of drug target proteins

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The genome project sequencing the increasing numbers of organisms are done and/or on going, and have changed the scale of biology. However, genome-sequencing projects are not an end in them. In fact, they only represent a starting point to understand the function of organism. A great challenge is how the expressions of thousands of genes can be characterized under physiological and pathological conditions, and how these patterns of expression define an organism.

There are two approaches that can be used to examine gene expression on a large scale available at this point. One uses nucleic-acid based technology, the other protein-based technology. Probably, the most promising nucleic-acid based technology might be differential display of mRNA, which uses polymerase chain reaction with arbitrary primers to generate thousands of cDNA species, each which correspond to an expressed gene or part of a gene. However, it is currently unclear if this technique can be developed to reliably assay the expression of thousands of genes or identify all cDNA species, and the approach does not easily allow systemic screening. Analysis of gene expression by the study of proteins present in a cell or tissue presents a favorable alternative. In contrast ot that, this purpose can be achieved by use of two-dimensional(2-D) gel electrophoresis, quantitative computer image analysis, and protein identification techniques to create a 'reference maps' of all detectable proteins. Such reference maps establish patterns of normal and abnormal gene expression in the organism, and allow examination of some post-translational modifications, which are functionally important for many proteins. It is possible to screen proteins systematically from reference maps to establish their identities.

To define protein-based gene expression analysis, the concept of the 'proteome' was recently proposed. A proteome is the entire **PTOT**eins complement expressed by a gen**OME**, or by a cell or tissue type. The concept of the proteome has some differences from that of the

genome, as while there change under different conditions, and can be dissimilar in different tissues of a single organism. A proteome nevertheless remains a direct product of a genome. Interestingly, the number of proteins in a proteome can exceed the number of genes present, as protein products expressed by alternative gene splicing or with different post-translational modifications are observed as separate molecules on a 2-D gel. As an extrapolation of the concept of the 'genome project', a 'proteome project' is research which seeks to identify and characterize the proteins present in a cell or tissue and define their patterns of expression.

Proteome projects present challenges of a similar magnitude to that of genome projects. Technically, the 2-D gel electrophoresis must be reproducible and high resolution, allowing the separation and detection of the thousands of proteins in a cell. Low copy number proteins should be detectable. There should be computer gel image analysis systems that can qualitatively and quantitatively catalog he electrophoretically separated proteins, to form reference maps. A range of rapid and reliable techniques must be available for the identification and characterization of proteins. As a consequence of a proteome project, protein databases must be assembled that contain reference information about proteins; such databases must be linked to genomic databases and protein reference maps. Databases should be widely accessible and easy to use.

The elements of proteome technology have existed in rudimentary form for almost two decades. Two-dimensional (2-D) gel technology has allowed the separation and display of complex mixtures of proteins and protein micro-characterization at the pico-mole level has become possible. However, it is only in the latter part of the 90's that this technology has been drawn together and refined in a form that enables analysis of complex biological systems be they organelles, cells, tissues, organs or indeed whole organisms. The paradigm of protein chemistry has now changed from purifying and characterizing proteins one at a time, to that of mass protein characterization after array of a complex sample. This is the proteomics revolution.

Recently, there have been many changes in the techniques and resources available for the analysis of proteomes. It is the aim of this symposium to dicuss the status of the areas of proteome projects, and to review briefly the progress of some current project, identification of drug target proteins from stomach cancer tissues.