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Application of Display Proteomics for the Development of Novel Biomarkers and Targets in Stomach Cancer

Chang-Won Lee* and Jae Won Kim

Laboratory for Proteome Analysis and Molecular Physiology, Genetic Engineering Institute/Division of Life Sciences, Gyeongsang National University, Jinju 660-701, South Korea

The completion of the sequencing phase of the human and mouse genomes provides the opportunity for describing human diseases in terms of complete network perturbations instead of indivisual genes and proteins. Proteomics is a technology-oriented science that studies protein expressions on a global scale. However, it is not yet known which components of proteomic profiles are biologically relevant for human disease networks in different individuals or which are excellent therapeutic targets for a given disease, except for already available drug targets. Hence the first task is a diagnostic one; to obtain the proteomic profiles of normal and diseased tissues and to biologically ascertain which protein combinations are the key contributors to these two categories in the specific genetic background of an individual. The molecular approach to disease analysis currently relies upon: 1) high-throughput microarray-driven differential display trascriptomics of diseases; 2) the analyses of single nucleotide polymorphisms (SNPs) in different human populations; 3) the proteomic approach involving gel-based and mass spectrometry-based differential display to uncover proteins whose levels and posttranslational modifications differ between diseased and normal tissues; 4) combinatorial chemistry-based approach to rapidly identify specific small molecules such as RNA aptamers and nonpeptides.

We have begun to set up, since 1998, the two-dimensional gel electrophoresis and mass spectrometry platforms for proteome analysis in Gyeongsang National University. Application of proteome analysis to the gastric carcinoma tissues from Korean patients began last year, and revealed several proteins that are potentially related to the disease state of gastric cancer. Tissue specimens were collected from patients who underwent gastric cancer surgery between 1999-2001 in Gyeongsang National University Hospital and Inha University Hospital. Matched normal tissues were used as controls. Protein extracts were prepared from both diseased and normal tissues, and proteins were displayed by two-dimensional gel electrophoresis. After visualization of protein spots either by Coomassie or silver nitrate, digital gel images obtained by scanner were analysed by PDQuest software and the results confirmed visually. Interesting spots were excised from the gel and digested with trypsin. The peptides were extracted and masses were determined by MALDI-TOF DE spectrometry. Protein identification was performed by peptide mass fingerprinting by searching the publically available protein databases with the determinded mass values as input. Some of the results obtained in our laboratory will be presented.

We will also briefly present the efforts of other proteomics laboratories to discover new biomarkers in various cancers, and discuss the expectations and realities of proteomics approach in discovering biomarkers and therapeutic targets.