Proteome Profiling of Post-Translational Modifications Using Ion-trap LC-MS/MS and Protein Biomarker Development Using Triple Quadrupole LC-MS/MS

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MS-based proteomics database can provide with global proteome abundances, targeted pathway data, global PTM pattern, and protein interactions, which will lead to phenome database such as molecular phenotype, cellular phenotype, and organismal phenotype. Especially, it provides accurate, quantitative data for a system biology view of cellular processes. We used several different types of LC-MS/MS for proteomics study.

Proteomics generally uses "Ion trap LC-MS/MS", which measures Precursor Ion (MS) & Fragmentation Ion (MS/MS) and extract information of identification and quantitation. Mostly used LC-MS/MS method is shotgun proteomics or bottom-up approach. For example, Peptide preparation ➔ Analysis with chromatography ➔ Analysis with mass spectrometry ➔ Database search ➔ Protein ID & quantitation**.** The other method is top-down approach, next-generation proteomics. It uses whole protein w/o generating peptides, which eventually bring richer information in whole protein itself.

MS-based proteomics can provide global information for post-translationa modifications (PTMs) such as phosphorylation, glycosylation, acetylation, methylation, ubiquitination and so on. It would provide information for whatever it can make mass difference. For example, comprehensive profiling of phosphoproteome in pancreatic beta cell was carried out. 6,277 unique phosphopeptides from 2,334 phosphoproteins were identified using 24 LC–MS/MS runs, with a 1% FDR at the peptide level. 683 phosphorylation sites are novel sites out of 2,467 unique phosphorylation sites. Some phospho-sites are shown in GTPase family and TF such as pdx-1, Nkx2.2, and Srebf1. Identified phospho-proteins are located in signaling pathways of beta-cell for signaling study.

Next, we applied Triple quadrupole LC-MS/MS (Multiple Reaction Monitoring, MRM) to verify cancer biomarkers in individual serum samples from 3 groups: healthy control group, liver cancer group, and recovered HCC group. After determining the relative quantities of the candidate proteins by MRM, we compared their expression levels between the 3 groups, identifying several potential biomarkers. The combination of multi-markers improved the discrimination of patient group versus the healthy control group compared with clinically used marker. We conclude that the combination of global data mining and LC-MS/MS enhances the screening and verification of potential cancer biomarkers.

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2. Education and Professional Career

Year	Institute	Position
1978-1982	서울대학교 공과대학 화학생물공학부	공학사
1982-1984	KAIST 생명과학과	이학석사
1987-1992	University of Texas at Austin, Dept. of Chem/Biochem	PhD
1992-1994	Yale University	Post-doc
1994-1999	영남대학교	부교수
1999-2001	University of Washington, School of Medicine	staff
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3. Recent Publications

[1] Development of Biomarkers for Screening Hepatocellular Carcinoma Using Global Data Mining and Multiple Reaction Monitoring, **PLOS ONE**, 2013, dx.plos.org/10.1371/journal.pone.0063468

[2] Verification of multimarkers for detection of early stage-diabetic retinopathy using multiple reaction monitoring **J. Proteome Res.**, 12(3) 1078-1089, DOI: 10.1021/pr3012073

[3]Retinal Proteome Analysis in a Mouse Model of Oxygen-Induced Retinopathy, **J. Proteome Research**, 11(11):5186-203, doi:10.1021/pr300389r