Department of Molecular & Cellular Bioanalysis

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Research Projects:

We have advocated elucidating the cellular functions through the measurement of biomolecules based on analytical chemistry. In particular, we have focused on proteome science consisting of mass spectrometry, nano-separation science, computational science and cell biology to develop the methodologies for the functional analysis of cells. More specifically, we are conducting research on the following five topics;

1) Development of novel analytical technologies for proteomics
2) Functional analysis of human proteomes by high resolution LC/MS/MS
3) Elucidation of intracellular phosphorylation network analysis
4) Intelligent proteome analysis by biomolecular mass spectrometry integrated with statistical signal processing
5) Metaproteome analysis of microbiomes in human diseases

Unlike genomic and transcriptomic researches, proteomics is still immature in terms of the measurement technologies and the complete analysis of proteome has not been established yet. The final goals of proteomics are to uncover the cellular protein events such as (1) protein expression/degradation, (2) protein localization, (3) protein interaction, (4) protein post-translational modifications (PTM) and (5) protein processing/splicing in proteome-wide.

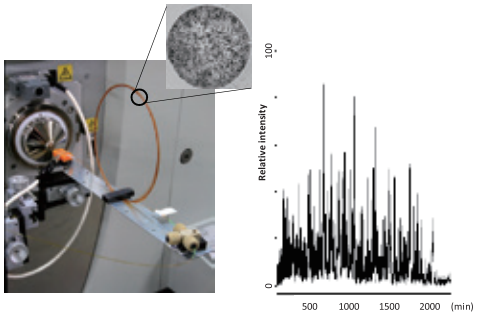

Figure 1 Complete proteome analysis by nanLC-MS.
(Left) nanoLC-MS system with 3.5 meter monolithic silica column. (Right) Total ion current chromatogram of E. coli proteome. Analysis on a microarray scale was achieved

We are aiming to develop novel approaches to tackle the technical barriers and to explore proteomic researches for clarifying the biological problems. In order to analyze the entire proteome expressed in cells, we are focusing on developing efficient separation systems based on nanoLC-MS using meter-long monolithic silica capillary columns with the world's highest performance beyond theoretical plate number 1,000,000. So far, our systems allowed to expand the measurable dynamic range of highly complex proteomics samples, achieving the analysis of Escherichia coli expressed proteome on a microarray scale (see Figure1). This system is currently applied to more complex proteome such as human.

We are also developing new technologies for quantitative proteomics by integrating intelligent statistical and bioinformatics approaches. In parallel, we built a public repository and database for proteomics datasets named jPOST and are collecting a variety of datasets acquired in world-wide, which are re-analyzed by the standardized approach and are shared with researchers according to open science policy.

In cellular signal transduction network, reversible phosphorylation is one of the key events to transduce the signal into nucleus to control the gene expression. Approximately 90% of human proteins were estimated to be phosphorylated. We have developed a highly selective enrichment method for phosphopeptides and applied to proteome-wide acquisition of cellular phosphorylation status. Currently we are working to intertwine the kinases with their substrates for revealing the whole picture of signaling network by using experimental and computational approaches.

Our proteomics system has been also employed to carry out metaproteome analysis of microbiomes in human gut, faces and oral environments to study several human diseases through the interaction between the bacteria and the host.

Recent publications

- Moriya et al., The jPOST environment: an integrated proteomics data repository and database. *Nucleic Acids Res.* **47** (D1), D1218-24, 2019.
- Tsai et al., Large-scale determination of absolute phosphorylation stoichiometries in human cells by motiftargeting quantitative proteomics. *Nat. Commun.*, **6**, 6622, 2015.
- Yamana et al., Rapid and deep profiling of human induced pluripotent stem cell proteome by one-shot nanoLC-MS/MS analysis with meter-scale monolithic silica columns. *J. Proteome Res.* **12**, 214-21, 2013.
- Imami et al., Temporal profiling of lapatinib-suppressed phosphorylation signals in EGFR/HER2 pathways. *Mol. Cell. Proteomics* **11**, 1741-57, 2012.