26G-ISMS38 **System-wide Temporal Characterization of the Phosphoproteome of Non-small-cell Lung Cancer Cells Treated with Erlotinib**

○ Adachi JUN[1], Yuichi ABE[1], Maiko SHIMIZU[1], Marina KISHIDA[1], Ayako SATO[1], Takeshi TOMONAGA[1]

[1]Laboratory of Proteome Research National Institutes of Biomedical Innovation, Health and Nutrition

Phosphoproteome is one of key signatures to understand the mode of action and mechanism of drug resistance of kinase inhibitors at the molecular level, pathway level and system level. We developed sensitive and high-throughput phosphoproteome and tyrosine phosphoproteome analysis platform and performed temporal characterization of non-small-cell lung cancer cell lines treated with erlotinib.

We obtained phosphoproteome and phosphotyrosine-proteome profiles of two erlotinib-sensitive cells and four erlotinib-resistant cells treated by erlotinib for 0 h, 6 h and 24 h. We quantified over 12000 phosphorylation sites by phosphoproteome analysis and over 600 phosphorylation sites on tyrosine residue by phosphotyrosine-proteome.

We extracted kinases and other enzymes which are up-regulated in resistant cells and selected 46 inhibitors for drug screening. 24 of 46 inhibitors inhibited cell growth of at least one resistant cell line.

Our sensitive and high-throughput phosphoproteome and tyrosine phosphoproteome analysis platform has a potential to identify pharmacoproteomic markers of drug efficacy as well as candiates of molecular targets to overcome drug resistance.