4A-O1-P-0900

様々なリン酸化プロテオミクス技術を用いたタンパク質キナーゼの標的基質の大規模同定と機能解析

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Global Identification and Functional Characterization of Protein Kinase Substrates using Various Phosphoproteomic Technologies

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Keywords: Phosphorylation, Protein Kinase, Cell Signaling, Phosphoproteomics, LC-MS/MS

Protein phosphorylation by protein kinases is one of the most widespread types of post-translational modifications in eukaryotes and can reversibly regulate diverse properties of proteins. Protein kinases are encoded by over 500 genes in higher eukaryotes and play critical roles in various cellular signaling pathways. In fact, many diseases such as cancer, metabolic disorders, and neurodegenerative diseases are associated with mutations in protein kinases. To fully and therapeutically understand the complex phosphorylation-mediated signaling networks, it is essential to develop analytical strategies for the global identification and functional characterization of *in vivo* substrates of individual protein kinases.

We have developed and adopted various phosphoproteomic approaches such as IMAC/2D-DIGE/MS[1)], TMT/IMAC/LC-MS, Phospho-PRM, and Phos-tag PAGE. These approaches have enabled efficient identification of protein kinases substrates and their phosphorylation sites in cells. Here we present physiological functions of the newly identified substrates of several disease-associated protein kinases including ERK[2)], PKD[3)], TBK1[4)], and PINK1[5)].

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