★Stem Cell Biology Seminar★

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Post-translational modifications in cancer metabolism

日時：2018年6月14日(木)15:00～16：00

会場：研究所B1F中会議室 (★皆様のご参加をお待ちしております★)

【講演要旨】The Hitosugi Laboratory at Mayo Clinic focuses on molecular mechanisms underlying how metabolism is regulated by oncogenic or tumor suppressive signaling that often causes imbalances in posttranslational modifications (PTMs) in human cancer. We employ proteomics- and GC/MS-based metabolic flux/metabolomics approaches to study molecular mechanisms of the interplay of dysregulated signaling pathways and metabolic pathways in cancer. We have identified previously unknown links between receptor kinase signaling and cell metabolism, including evidence that oncogenic HER2 signaling activates a pathway that transfers energy from mitochondria to the cytosol by stabilizing Mitochondrial Creatine Kinase (MtCK) 1 through tyrosine phosphorylation, thereby fulfilling bioenergetic needs in the cytosol for rapid proliferation of breast cancer cells. This study not only deciphers the molecular mechanism underlying the intersection between HER2 signaling and mitochondrial energy transfer, but also demonstrates that targeting this energy transfer pathway using the dietary supplement creatine analogue, cyclocreatine suppresses proliferation of HER2+ cell lines, including trastuzumab-resistant lines, and reduces tumor growth in vivo without any obvious toxicity. In addition, we have recently identified carnitine palmitoyltransferase (CPT)1A as a first mammalian mitochondrial lysine succinyltransferase that succinylates substrate proteins at lysine residues, which is a significant breakthrough in regulation of a novel PTM, lysine succinylation.

【関連文献】

1) Kurmi et al., **Cell Reports** 22:1365-1373, 2018
2) Hitosugi et al., **Nat Commun** 4:1790, 2013
3) Hitosugi et al., **Cancer Cell** 22:585-600, 2012
4) Hitosugi et al., **Mol Cell** 44:864-877, 2011

主催：生体恒常性プロジェクト (連絡先：田久保 圭誉・内線2875)