FBS・医学系研究科 セミナー

～革新的がん治療法を大学から世界へ～

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生命機能研究科 システム棟　2階セミナー室

“Combating Cancer with a Powerful Chemical Genetics Approach and Model Systems”

＜Abstract＞

Mitogen-activated protein kinases (MAPKs), found in all eukaryotes, are signal-transducing enzymes playing a central role in a variety of biological processes, such as cell proliferation, survival and differentiation. Aberrant regulation of MAPK cascades contributes to cancer and other human diseases, thus posing the ERK MAPK pathway as a promising target for therapeutic intervention in cancer. This study builds on our previous works on the discovery and intensive research efforts on the regulatory mechanisms of the MAPK signaling pathway in fission yeast. The myriad genetic resources available to study wide-ranging mutant phenotypes, combined with the high degree of conservation of basic signaling pathways, render the yeast model systems particularly invaluable for studies of cellular pharmacology and cancer therapeutics (Cancer Cell 2002).

We have discovered the Pmk1 MAPK signaling pathway and demonstrated that Pmk1 MAPK and the phosphatase calcineurin act antagonistically in the Cl- homeostasis in fission yeast. Based on the functional interaction between calcineurin and MAPK, we have developed several genetic screens, which efficiently identified negative regulators, activating regulators as well as targets of the Pmk1 MAPK pathway.

As MAPK signaling pathways are one of the most attractive targets for cancer therapy, inhibitors that target this signaling pathway appear to be promising drug candidates for the treatment of cancer. Here, I first give an overview of the use of fission yeast as a model system for drug discovery and then, I introduce our molecular genetic strategy to identify regulators of MAPK signaling and the application of this approach to drug discovery. Remarkably, one of the hit compounds SK-II identified in our chemical genomics screen inhibited proliferation of several tumor cell lines and the ERK MAPK and the PDK/AKT signaling pathways by targeting as-yet unidentified molecules. Our chemical genetics screen thus provides a novel and innovative therapeutic approach for cancer

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