S13-5 A novel strategy for systematic identification of intracellular targets of bioactive natural products

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Identification of the molecular targets for bioactive small molecules provides deep insights into drug discovery and development. Recently, much attention has been drawn to chemical genetics, in which mutations in classical genetics are replaced by small-molecules, as a method for drug target identification. We have identified several important regulators including histone deacetylase as such the specific targets for anticancer natural products by the chemical genetic approach. Development of the methodology for systematic identification of the drug-target interaction will be important for establishing chemical genomics. However, it is sometimes difficult to determine the targets using the physical interaction, due to low affinity to the target and the decrease in activity by the modifications for probe synthesis. On the other hand, a genome-wide screening of genetic interaction has become available for understanding the mechanism of action. We have obtained a whole ORF library (ORFeome) of fission yeast and performed a variety of reverse proteomics including a global analysis of subcellular localization (localizome). The usefulness of the fission yeast reverse proteomics for target identification will be discussed.