Chemical probes for the modulation of phosphatase activity

Maja Köhn

European Molecular Biology Laboratory,
Genome Biology Unit, Heidelberg, Germany
koehn@ embl.de

Within intracellular signaling networks, phosphatases are counter players of kinases and play crucial roles in health and disease. The investigation of phosphatases is challenging, which is also due to the lack of tools to selectively study particular phosphatases. Understanding of phosphatase function, regulation and substrate interaction is therefore still quite limited.

The development of chemical modulators of phosphatases, that is activators or inhibitors, faces several difficulties. Active site inhibitors are hardly selective due to structurally conserved active sites. They are also rarely bioavailable because phosphatases prefer to bind negatively charged molecules, which is due to their substrates being phosphorylated proteins or second messengers. For the design of chemical activators no general strategies are available, and allosteric sites that can be used for this purpose need to be identified.

I present here approaches for the design of specific chemical activators and inhibitors of protein phosphatases that are based on the natural interaction partners of phosphatases and are active inside cells.