Protein Dynamics and Flexibility by NMR

Mini-Symposium

Functional disorder and dynamics in soluble and membrane proteins involved in cell signalling

IBS Seminar room

December 11th

10.30 - Intrinsic disorder in membrane proteins - roles in regulation and scaffolding with links to phosphorylation**.**
Professor Birthe B. Kragelund University of Copenhagen

11.15 - Dynamic Regulation of Enzymes.
Professor Wolfgang Peti Brown University

All are welcome

Intrinsic disorder in membrane proteins

roles in regulation and scaffolding with links to phosphorylation

Professor Birthe B. Kragelund
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Abstract

Intrinsically disordered regions (IDRs) in membrane proteins play central roles in cellular signaling processes and like their structured protein counterparts, they engage in interaction networks of regulatory nature. Intracellular domains of many membrane proteins contain large IDRs of importance for function and with numerous predicted as well as confirmed phosphorylation sites. Due to their lack of globular structure insight into their structure-function relations have been crucially lacking. Using NMR spectroscopy, biophysics and cell-biology we have deciphered regulatory roles of intrinsic disorder in cytokine receptors and in ion transporters with direct links to phosphorylations. The interplay of intrinsic disorder and phosphorylation in these proteins highlights specific space and temporal effects in scaffolding including interplay with some of the major signaling pathways such as JAK2/STAT and MAPK-signaling.

Dynamic Regulation of Enzymes

Professor Wolfgang Peti,
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Abstract

Tyrosine phosphorylation fulfills essential biological functions. The catalytic mechanism of tyrosine phosphatases (PTPs) has been well studied and understood since ~20 years and is largely based on the nvestigation of 3-dimensional crystal structures of these enzymes. Indeed, numerous loops, including the WPD, the Q and the E-loop, among others, change their conformation depending on the state in the catalytic cycle. Critically, it has recently been shown that the catalytic turnover of PTP1B is directly determined by the speed of the WPD-loop motion. However, it has not been shown if there is an intrinsic regulatory element within PTPs that allows for modulation of the WPD-loop motion and thus controls PTP function.
Here we present that these intrinsic regulatory elements exist and put forward the idea of a connected communication within PTPs that controls the activity of their catalytic efficiency. This newly determined communication pathway, which is similar to that recently proposed for kinases, is a novel route to inhibit PTPs in a highly specific manner.