MPI-NAT SEMINAR SERIES

© Basil Greber

Basil Greber

The Institute of Cancer Research, London, UK

High-resolution structures of the human CDK-activating kinase bound to inhibitors: Harnessing the power of cryo-EM for discovery of cancer therapeutics

The human CDK-activating kinase (CAK) is a trimeric protein complex that acts as a master regulator of cell division and has been identified as a promising target for cancer therapy. Structural data are of great importance for the rational, structure-based design of next-generation therapeutics. Harnessing the power of cryo-electron microscopy (cryo-EM) for this task requires the development of workflows that enable structures of small, asymmetric complexes such as the human CAK to be determined at high resolution and with high throughput. To address these challenges, we initially determined structures of the human CAK bound to nucleotide analogues and inhibitors at up to 2.5 Å resolution. These results provided important insights into the molecular details of the assembly, activation, and inhibition of the human CAK. Recent work has now achieved the routine 2 Å-structure determination for the 85 kDa catalytic module of the human CAK bound to inhibitors, which provides us with new insights into CDK inhibitor selectivity.

Thursday, 18.04.2024, 11:00 am

Host: Kristina Žumer
Department of Molecular Biology

Faßberg Campus
Ludwig Prandtl Hall

MAX-PLANCK-INSTITUT
FÜR MULTIDISZIPLINÄRE
NATURWISSENSCHAFTEN