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COMBINING X-RAY AND CRYO-EM TO STUDY LARGE AND DYNAMIC MACROMOLECULAR COMPLEXES

Holger Stark

Max-Planck Institute for Biophysical Chemistry, Germany

Single particle cryogenic electron microscopy (Cryo-EM) has developed into a powerful technique to determine 3D structures of large macromolecular complexes. Due to improvements in instrumentation and computational image analysis, the number of high-resolution structures is steadily increasing. The method can not only be used to determine high-resolution structures but also to study the dynamic behavior of macromolecular complexes and thus represents a very complementary method to X-ray crystallography. We have recently determined the structure of human proteasomes and their inhibition by anti-cancer drugs using X-ray crystallography to visualize the chemistry of inhibition at an unprecedented resolution of 1.8 Å. By Cryo-EM, we were able to visualize the long-range allosteric conformational changes induced by the drug binding and visualized the effects of drug binding in terms of restrictions in the free-energy landscape of the human 26S proteasome. More examples of Cryo-EM studies of dynamic processes in large macromolecular complexes will be presented at the conference.

Biography

Holger Stark has studied Biochemistry and completed his PhD from the Free University of Berlin, Germany. After a short Post-doctoral study at the Imperial College London (UK), he became a Group Leader at the University of Marburg (Germany) and moved from there to the Max-Planck-Institute in Göttingen (Germany) where he later became the Director in 2015. He has over 100 publications and an H-index of 45.

hstark1@gwdg.de