LS.4.124

High Resolution Structure of the Mycobacterial Fatty Acid Synthase - Automated Image Acquisition on a Direct Electron Detector

D. Boehringer[1], N. Ban[1], M. Leibundgut[1]

[1]ETH Zurich, Institute of Molecular Biology and Biophysics, Zurich, Switzerland

Daniel.boehringer@mol.biol.ethz.ch
Keywords: mycobacterium, type I fatty acid synthase, single particle cryo-EM, mycolic acid biosynthesis

The mycobacterial fatty acid synthase (FAS) complex is a large, 2.0 megadalton, multifunctional enzyme that catalyzes the synthesis of fatty acid precursors to mycolic acids, which are major components of the cell wall in Mycobacteria and play an important role in pathogenicity.

Here we present the three dimensional reconstruction of the M. smegmatis FAS complex, highly homologous to the M. tuberculosis multienzyme, by cryo-electron microscopy [1]. Using a direct electron detector we obtained images with a high signal to noise ratio which allowed us to select images representing the main conformation of this heterogeneous macromolecular complex. The mycobacterial FAS structure resembles the cage like architecture of fungal FAS but exhibits larger openings and fewer stabilising linking elements. Based on the secondary structural elements present in the reconstruction, and sequence homology with the fungal FAS, we generated an accurate molecular model of the complex. Our reconstruction reveals structural features that may be important for the interaction with the mycolic acid processing and condensing enzymes that further modify the precursors produced by FAS.

1. D. Boehringer, N. Ban, M. Leibundgut, J Mol Biol. 425 (2013) p. 841