Sample Preparation for Cryo-EM: Challenges and Perspectives

Mathieu Botte, *leadXpro AG, Switzerland*

Abstract

Despite recent advancements in single particle cryo-electron microscopy (cryo-EM), limitations in feasibility and resolution of the analysis for small (<100 kDa) and asymmetric proteins have still yet to be overcome. One popular strategy aims at enlarging proteins by complexation with antigen-binding fragments (Fab) or nanobodies.

We developed the Pro-Macrobodies (PMbs) technology, which is a chaperone derived from nanobodies covalently and rigidly coupled to a MBP giving a weight of 55 kDa. Using two examples, we will demonstrate the benefits of this new technology for cryo-EM structure determination of challenging membrane protein drug targets.