BDR SEMINAR via Zoom

Shiwei Zhu

Yale University

Thursday, March 17, 2022

10:00-11:00

Zoom meeting URL will be announced on the event day by e-mail.

※This seminar is only for BDR members.

Cryo-ET Pipeline for Imaging Small Proteins in Large Biological Structures

Summary

All living organisms defend themselves against microbial infection in a process called cell autonomous defenses. Human guanylate-binding protein 1 (hGBP1), one of the interferon inducible effectors is the central player in the signaling of cell-autonomous defense since hGBP1 rapidly coats invasive bacteria inside human cells and creates a signaling hub that activates caspase-4-dependent cell pyroptosis. How this 68kDa hGBP1 protein is recruited to the bacterial surface, the mechanism of its self-assembly and the structure of the ensuing protein coat or "coatomer" are unknown. Here, we performed in situ cryo-electron tomography (cryo-ET) to resolve the structure of a massive antimicrobial complex generated by polymerization of 30,000 over the entire surface of Gram-negative bacteria within the host cell cytosol. Meanwhile, we constructed an ex-situ system to study the mechanism of hGBP1 targeting/coating the bacterial pathogen Salmonella typhimurium minicell. Cryo-ET found hGBP1 elongates ~280Å for bacterial membrane insertion to establish this platform, triggering lipopolysaccharide release that activates co-assembled caspase-4. Thus, we have built a platform that leverages the high resolution ability of an in vitro system with the native conformation only obtained in situ. The approach of in/ex-situ cryo-ET provides a new pipeline for studying small proteins at the host pathogen interface

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