生命科学セミナー

Towards structural cell biology using superresolution microscopy

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Abstract: Recent advances in superresolution microscopy now allow us to address structural questions in cell biology with optical methods. I will show how superresolution microscopy can be used to gain mechanistic insights into the structural organization of a complex protein machine, namely the machinery involved in clathrin-mediated endocytosis.

Clathrin-mediated endocytosis is an essential cellular function of all eukaryotes. It relies on a self-assembled macromolecular machine of over 50 different proteins in tens to hundreds of copies that mediate vesicle formation. How so many proteins can be organized to produce endocytic vesicles with high precision and efficiency is not understood. To address this gap, we developed high-throughput superresolution microscopy to reconstruct the nanoscale structural organization of 23 endocytic proteins from over 100,000 endocytic sites in yeast. This allowed us to visualize where individual proteins are localized within the machinery throughout the endocytic process.

By combining superresolution imaging, live-cell microscopy and Brownian dynamics simulations, we aim to identify the architectural features that allow the endocytic machinery to create vesicles with high efficiency and robustness. We found that actin filament nucleation is pre-patterned by a nucleation nanotemplate, which directly links molecular organization to the mechanics of endocytosis, and might represent a general design principle for directional force generation in other membrane remodeling processes such as during cell migration and division.

References:

Thevathasan et al. “Nuclear Pores as Versatile Reference Standards for Quantitative Superresolution Microscopy.” BioRxiv, 582668.

Mund et al. “Systematic analysis of the molecular architecture of endocytosis reveals a nanoscale actin nucleation template that drives efficient vesicle formation,” Cell, (2018).

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