SENSORS AND PROBES

Lipid biology in super-resolution

BODIPY dimerization is exploited for super-resolution imaging and single-particle tracking of lipids in living cells.

Single-molecule localization microscopy methods make use of fluorescent probes that switch between states, typically between on and off states or between different colors, for localizing individual emitters to generate a super-resolution image. Although this need for convertible probes has led to major advances in probe development, generally useful strategies for labeling biomolecules for localization microscopy are still needed.

Elias Puchner and his laboratory at the University of Minnesota have developed an approach that enables single-molecule imaging and tracking of lipids and fatty acids in living cells with BODIPY dyes. This work has potentially broad implications as hundreds of BODIPY-labeled probes have been developed that target a range of subcellular structures.

Their approach exploits the known observation that BODIPY dyes in close proximity can form ground-state dimers that are red-shifted relative to their monomeric counterparts. This red shift allows dimers to be imaged independently from the pool of labeled probes. Dimerization is concentration-dependent and stochastic, meaning that the density of dimers can be controlled for high-quality single-molecule imaging and tracking of abundance and diffusing molecules, such as certain types of lipids.

The team demonstrated the validity of this approach in yeast, where they could perform single-particle tracking of labeled molecules as well as localization microscopy with a resolution of ~30 nm. They further showed that the method is also applicable in mammalian cells. The researchers then examined fatty acid localization under various conditions in yeast. For this, they used analogs of fatty acids and neutral lipids labeled with red and green BODIPY, respectively, and studied their diffusion under well-fed and starvation conditions. In well-fed cells, both analogs showed free diffusion in the endoplasmic reticulum. However, when cells were starved, the analogs were confined to 100-nm regions that colocalize with the plasma membrane. These results suggest that spatial sequestration may protect against lipotoxicity during starvation. Taken together, their results highlight the power of using BODIPY dimerization to study lipids in cells in super-resolution.

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