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Abstract: 95O

Spatiotemporally Mapping Thermal Dynamics of Lysosomes and Mitochondria using Cascade Organelle-Targeting Upconversion Nanoparticles

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The intracellular metabolism of organelles, like lysosomes and mitochondria, are highly coordinated spatiotemporally and functionally. The activities of lysosomal enzymes significantly rely on the cytoplasmic temperature, and heat is constantly released by mitochondria as the byproduct of ATP generation during active metabolism. Here, we develop temperature-sensitive LysoDots and MitoDots to monitor the *in situ* thermal dynamics of lysosomes and mitochondria. The design is based on upconversion nanoparticles (UCNPs) with high-density surface modifications to achieve the exceptionally high sensitivity of 2.7% K^{-1} and accuracy of 0.8 K for nanothermometry to be used in living cells. We show the measurement is independent of the ion concentrations- and pH values. With Ca^{2+} ion shock, the temperatures of both lysosomes and mitochondria increased by 2~4 °C. Intriguingly, with Chloroquine treatment, the lysosomal temperature was observed to decrease by up to ~3 °C, while mitochondria remained relatively stable. Lastly, with oxidative phosphorylation inhibitor treatment, we observed a 3~7 °C thermal increase and transition from mitochondria to lysosomes. These observations indicate different metabolic pathways and thermal transitions between lysosomes and mitochondria inside HeLa cells. The nanothermometry probes provide a powerful tool for multi-modality functional imaging of subcellular organelles and interactions with high spatial, temporal and thermal dynamics resolutions.

Key Words: Lysosome, Mitochondria, Nanothermometry, Upconversion Nanoparticles (UCNPs)
Ref 1 Di et al *Nano Letters* 2021
Ref 2 Di et al *PNAS*, under revision 2022