Temporal, Spatial and Thermal Dynamics of Intracellular Organelles Revealed by Biophysical Nanotools and Advanced Imaging

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The intracellular metabolism of organelles, like lysosomes and mitochondria, is highly coordinated spatiotemporally and functionally [1, 2]. The activities of lysosomal enzymes significantly rely on the cytoplasmic temperature, and heat is constantly released by mitochondria as the byproduct of adenosine triphosphate (ATP) generation during active metabolism. Here, we developed temperature-sensitive LysoDots and MitoDots to monitor the in situ thermal dynamics of lysosomes and mitochondria [3, 4]. The design is based on upconversion nanoparticles (UCNPs) with high-density surface modifications to achieve the exceptionally high sensitivity of 2.7% K21 and low uncertainty 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 Ca2+ ion shock, the temperatures of both lysosomes and mitochondria increased by ∼2 to 4 °C. Intriguingly, with chloro- quine (CQ) 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 an ∼3 to 7 °C temperature increase and a thermal 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.

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