

MitoAtlas, a Mitochondrial Proteome Map Created with Super-Resolution-Proximity-Labeling

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Abstract: We employed super-resolution proximity labeling (SR-PL) method with APEX2 and BioID to map the sub-mitochondrial proteome of HEK293T-REx cells, generating extensive data on 13,348 biotin or DBP-modified sites. Using machine learning, we classified 11,660 sites into distinct sub-mitochondrial spaces. This led to the development of MitoAtlas, a comprehensive proteome map of 858 mitochondrial proteins with detailed sub-mitochondrial localization and topological information. We also identified 120 mitochondrial orphan proteins. By computational analysis, it was shown that local factors of the reactive residues affect the labeling reaction of APEX2 and BioID in different ways. Specific bait-prey pairs were modeled with AlphaFold-Multimer for finding potential protein interactions. Further SR-PL investigation showed how PEX3 and PEX16 KO affects the mitochondrial proteome and protein import of HEK293T-REx cells at the super-resolution level. To facilitate public access, we created a website (mitoatlas.org) containing extensive information on these proteins.

