MOF acetyl transferase maintains mitochondrial homeostasis

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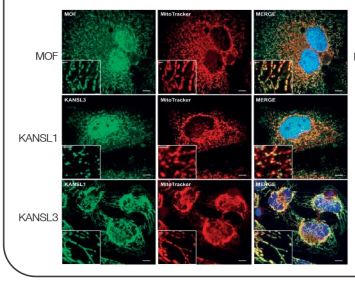
Abstract

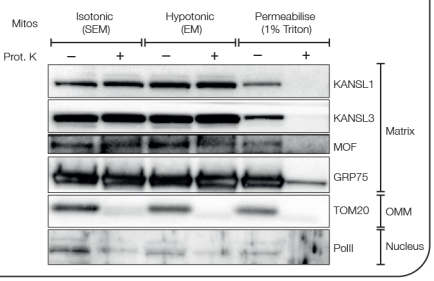
Mitochondrion lies at the centre of cellular and organismal energy homeostasis, housing a large repertoire of enzymes that are required for the synergy of vrious metabolic pathways. Mitochondrial gene expression and protein acetylation are two important fundamental processes situated at the crossroad between mitochondrial function and metabolic status of a cell. MOF acetyl transferase and its KANSL complex members dually localize to the nucleus and the mitochondria in mouse and human cells. The MOF-KANSL complex regulates metabolic gene transcription in the nucleus and expression of Electron Transport Chain (mtETC) components from the mtDNA, in a media and cell type dependent fashion. Regulation of nuclear gene transcription by MOF is well understood, however, its control of mitochondrial function remains elusive. Here, we report that loss of MOF leads to severe mitochondrial dysfunction in Mouse Embryonic Fibroblasts (MEFs), sprouting from a stalled oxidative phosphorylation. We address the mechanisms by which the enzyme maintains mitochondrial function in these cells by using approaches to detect transcriptional and post-transcriptional changes. Collectively our data suggest that MOF has emerged as a moderator to strike a balace in the context of communication between the nucleus and the mitochondria.

MOF-KANSL complex members localise to the mitochondria

Immunofluorescence on Hela cells

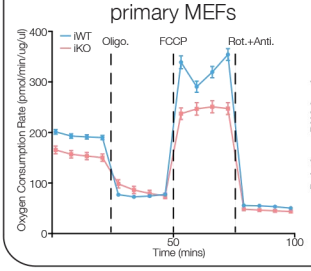


Proteinase K protection assay on primary MEFs

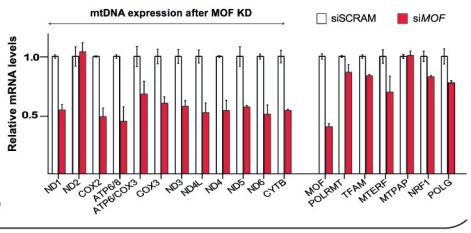


MOF depletion affects mitochondrial respiration and mtDNA transcription

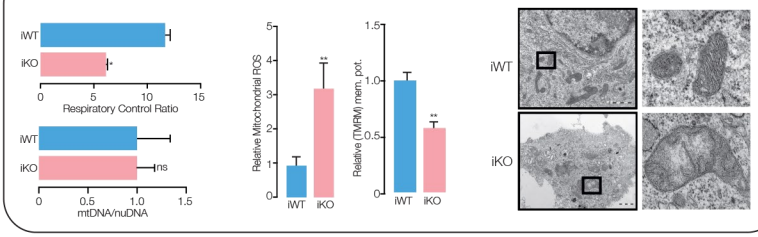
Seahorse Mito Stress Test on primary MEFs



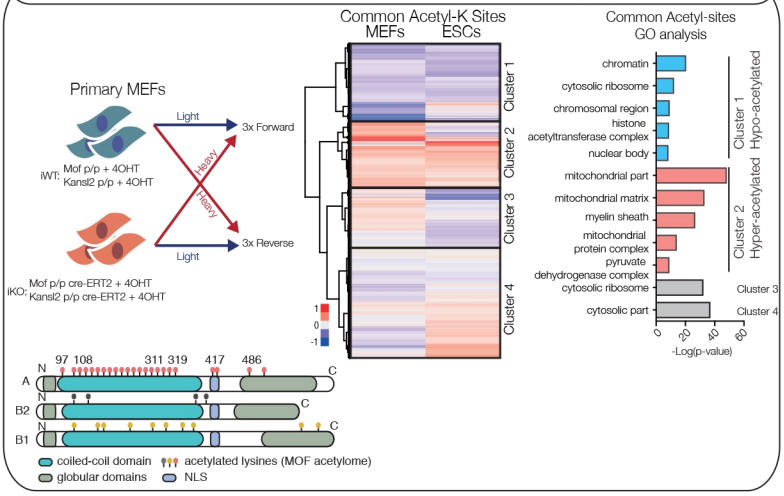
RT-PCRs on galactose adapted Hela cells



MOF depletion causes mitochondrial dysfunction

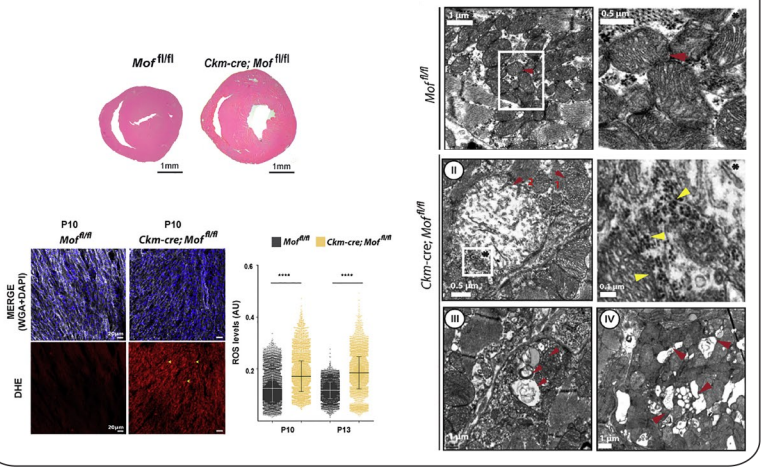


MOF and KANSL2 acetylate non-histone proteins

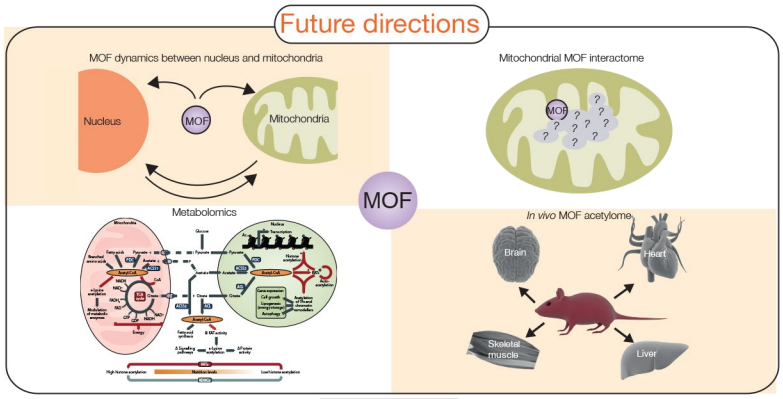


MOF depletion affects mitochondria *in vivo*

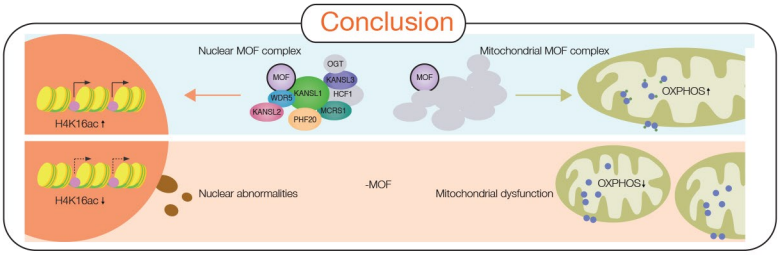
Mouse cardiac muscle



Future directions



Conclusion



References

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(3) Sheikh & Akhtar.The many lives of KATs-detectors,integrators and modulators of the cellular environment. Nat. Rev. Genet. (2018)
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