



## CLUH couples mitochondrial distribution to the energetic and metabolic status

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Titre CLUH couples mitochondrial distribution to the energetic and metabolic status

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Résumé en anglais Mitochondrial dynamics and distribution are critical for supplying ATP in response to energy demand. CLUH is a protein involved in mitochondrial distribution whose dysfunction leads to mitochondrial clustering, the metabolic consequences of which remain unknown. To gain insight into the role of CLUH on mitochondrial energy production and cellular metabolism, we have generated CLUH-knockout cells using CRISPR/Cas9. Mitochondrial clustering was associated with a smaller cell size and with decreased abundance of respiratory complexes, resulting in oxidative phosphorylation (OXPHOS) defects. This energetic impairment was found to be due to the alteration of mitochondrial translation and to a metabolic shift towards glucose dependency. Metabolomic profiling by mass spectroscopy revealed an increase in the concentration of some amino acids, indicating a dysfunctional Krebs cycle, and increased palmitoylcarnitine concentration, indicating an alteration of fatty acid oxidation, and a dramatic decrease in the concentrations of phosphatidylcholine and sphingomyeline, consistent with the decreased cell size. Taken together, our study establishes a clear function for CLUH in coupling mitochondrial distribution to the control of cell energetic and metabolic status.

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## Liens

- [1] <http://okina.univ-angers.fr/publications?f%5Bauthor%5D=28485>
- [2] <http://okina.univ-angers.fr/publications?f%5Bauthor%5D=28486>
- [3] <http://okina.univ-angers.fr/publications?f%5Bauthor%5D=15968>
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- [18] <http://okina.univ-angers.fr/publications/ua17103>
- [19] <http://dx.doi.org/10.1242/jcs.201616>
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