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ELOINA CORRADI

LIPhy, Grenoble, France

**MECHANO-INDUCED MITOCHONDRIAL
MORPHO-FUNCTIONAL REMODELING**


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Mitochondria are double-membrane organelles that, among other functions, sustain the bioenergetic metabolism of cells by producing ATP at the level of the cristae. ATP production efficiency and mitochondrial morphology are tightly linked. Mitochondrial morphological adaptability is ensured by the continuous transitioning between fission and fusion, phenomena which rely on specific proteins, but also membrane contact sites. By being coupled to mitochondrial functions, the reshaping of mitochondria across spatial scales regulates the cellular bioenergetic and metabolic states.

Mechanical stimuli have recently been shown to modulate cellular metabolism, thus impacting physiological (e.g. cell migration, proliferation, death) and pathological (e.g. cancer progression) processes. We thus investigated the mechano-driven reshape of mitochondria, as a mechanism to modulate bioenergetic metabolism. By using a unique biomechanical tool to stretch cells compatible with super-resolution microscopy, we were able to show that mechanical stimulation drastically re-shape mitochondria across spatial scale. Indeed, a single mechanical stretch reshaped these organelles both at the macro and nanoscale. In particular, mechanical stretch triggers mitochondrial fission, passing through nanoscale deformation of the outer membrane, and a reshape of the inner membrane architecture.

Overall, we show how mechanical forces reshape mitochondria at a spatiotemporal resolution never tackled before, further opening the horizon of mechano-metabolism based on cellular organelle re-shaping.

Invited by : Monika Dolega

 Twitter : IAB_Officiel
Website : <https://iab-grenoble.fr/>