Body

CRISPRi Screen Discovers Mitochondrial Distress Signal

The function of mitochondria, the ?powerhouse of the cell,? can be compromised in aging and disease. Dysfunctional mitochondria trigger a global cellular stress response, but how human mitochondria signal stress to the rest of the cell was unknown.

In a project led by postdoc Xiaoyan Guo in the Kampmann lab [1], a CRISPRi-based genetic screen uncovered the molecular mechanism by which mitochondrial dysfunction is relayed to the rest of the cell. The mitochondrial protease OMA1 cleaves a previously little characterized protein, DELE1. Cleaved DELE1 activates the kinase, HRI, triggering the so-called integrated stress response.

This newly discovered OMA1?DELE1?HRI pathway is a potential therapeutic target in diseases that involve mitochondrial dysfunction, such as neurodegenerative diseases or heart disease.

The article describing these results was published in the March 4, 2020, issue of Nature:

Guo X, Aviles G, Liu Y, Tian R, Unger BA, Lin YT, Wiita AP, Xu K, Correia MA, Kampmann M (2020) Mitochondrial stress is relayed to the cytosol by an OMA1-DELE1-HRI pathway. Nature 579: 427?432. [2]

Read the UCSF news release here. [3]

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Links
[1] https://kampmannlab.ucsf.edu/
[2] https://www.nature.com/articles/s41586-020-2078-2
[3] https://www.ucsf.edu/news/2020/03/416856/cellular-sos-crispr-technique-reveals-how-cells-power-plants-activate-emergency