UNIVERSITÉ DE GENÈVE

PRESS RELEASE

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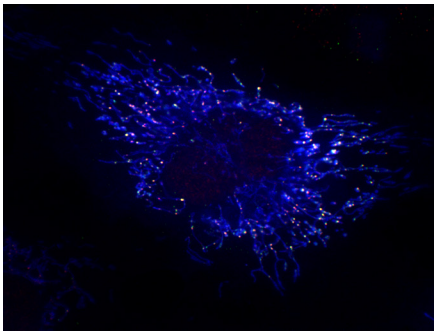
How cells optimize the functionning of their power plants

Researchers at UNIGE, Switzerland, uncover veritable 'assembly plants' in mitochondria, the organelles responsible for energy production.

Mitochondria, which are probably derived from distant bacterial ancestors incorporated into our cells, have their own DNA. However, we know little about how these organelles, which convert oxygen and consumed nutrients into energy, regulate the expression of their own genes. Jean-Claude Martinou, professor at the University of Geneva (UNIGE), Switzerland, and his team, have discovered the existence of compartments at the heart of mitochondria, consisting of hundreds of different proteins. It is here that RNA molecules (the many copies made from DNA) come together to be processed and begin their maturation. Equipped with enzymatic hardware of all sorts, these assembly plants, named 'mitochondrial RNA granules', are described in the journal *Cell Metabolism*. Many pathologies associated with mitochondrial disorders may be caused by dysfunctional mitochondrial RNA granules.



A human cell whose nucleus is surrounded by mitochondria (blue fluorescence). The presence of mitochondrial RNA (red) in the granules (green) results in a combined fluorescence ranging from pink to yellow.
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Mitochondria, present in varying numbers in each of our cells, are true power plants. These organelles actually produce energy from the combustion of nutrients, to be used by the cell to perform its daily tasks. Unlike other cell organelles, which are only subject to the laws dictated by the cell's DNA, mitochondria possess their own genome. This is probably the result of a symbiosis, which occured during the course of evolution, between their distant bacterial ancestors and cells of that time.

'All in one' transcription of DNA

Human mitochondrial DNA codes specifically for various proteins involved in the molecular equipment used to produce energy. This genetic material is transcribed into long RNA molecules - copies - which are comprised of both instructions for making proteins and the 'tools' to assemble them. This type of layout, in the form of an 'all in one kit', represents another bacterial atavism.

"We don't really know how mitochondria regulate the expression of their genes. These long precursor RNA molecules, which do not exist anywhere else in the cell, must be processed in a distinctive way, with machinery specific to this organelle", reveals Jean-Claude Martinou, professor in the Department of Cell Biology, of the Faculty of Science. In collaboration with researchers from the University of Newcastle, his team has taken on the task of elucidating this type of structure.

Diseases linked to mutations in mitochondrial DNA

"Specifically, we tracked RNA molecules that we rendered fluorescent and observed their convergence and accumulation in previously un-

known compartments" reports Alexis Jordan, a member of the group and first author of the article. "Made up of hundreds of different proteins, these are relatively large structures." Among these proteins are several enzymes known to play a role in the transformation of RNA into active entities. The precursor RNA molecules gathered in these compartments are thus sliced into sections corresponding to their various components: the instructions for building each protein, and the various 'tools' used to assemble them.

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"These assembly plants, which concentrate the machinery to process RNA, were baptized 'mitochondrial RNA granules'. It is now possible to explore in more detail the different stages of mitochondrial RNA maturation and to understand its mechanism", explains Jean-Claude Martinou, an assertion whose importance is underlined by the fact that different pathologies are associated with dysfunctions in the processing of this RNA. The researchers intend to determine whether mutations in the RNA granule machinery are involved in the development of some of these diseases.

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