MedicalXpress

Mitochondria adopt a crosswise pathway for decoding their genome

February 19 2015

Mitochondria, true energy power plants of cells, are able to release the energy contained in food by means of the oxygen which we inhale. These intracellular organelles possess their own DNA, and proteins derived from these genetic instructions are produced according to a specific process, which is not well known. Misregulation of this process can cause mitochondrial genetic diseases in humans.

Now, the team of Jean-Claude Martinou, professor at the Faculty of Science of the University of Geneva (UNIGE), Switzerland, discovered a new component of the process, unheard of in mammals. It relates to the biogenesis of ND6, a protein essential for the mitochondrial activity. Described in detail in the journal *Cell Reports*, these data provide insights into the general process of mitochondrial RNA maturation.

The food we consume is converted into energy within mitochondria, organelles present in each of our cells. These tiny energy power plants produce themselves part of the proteins involved in this task, using the instructions contained in their own DNA. Their genetic material is transcribed into long RNA molecules - copies - that must be processed following specific rules, peculiar to mitochondria. "We had previously discovered the existence of compartments to which RNA molecules converge, to be treated and begin their maturation. The next step was to acquire a better understanding of this process, the defects of which are often the cause of mitochondrial genetic diseases in humans", explains Jean-Claude Martinou, professor in the Department of Cell Biology of the UNIGE.

A mechanism unheard of in mammals

In association with researchers of the universities of Angers (France), Valladolid (Spain), Madrid (Spain) and Boston (United States), the Geneva team studied the RNA maturation of ND6, a key-protein of the molecular machinery necessary to produce energy. The biologists unveiled a new process in mammals. "We discovered that a protein called FASTK also exists in a form capable of penetrating into mitochondria. Once it reaches a compartment of maturation, this protein binds diverse regions of the ND6 RNA. The physical protection provided by FASTK thus prevents the action of the degradosome, an enzymatic complex whose task is to digest the extremities of RNA", says Alexis Jourdain, first author of the article. This type of mechanism of protection was already known in plants, but its existence in mammals was so far unreported.

The energy-consuming organs are the most affected

The protein FASTK plays a key-role in the process of biogenesis of ND6. If the RNA coding for this protein does not reach maturation, all the respiratory chain of the mitochondrion is affected. "There is a mutation in a gene coding for a protein related to FASTK, which is associated with a form of infantile mitochondrial encephalomyopathy ", reports Jean-Claude Martinou. The precise mechanism underlying the pathology associated with this mutation remains however to be established. The group of experts is currently developing an animal model of this disease and thus hopes to understand the defective mechanisms occurring in those patients.

Provided by University of Geneva