Cannabidiol demonstrated to alleviate symptoms of Leigh syndrome

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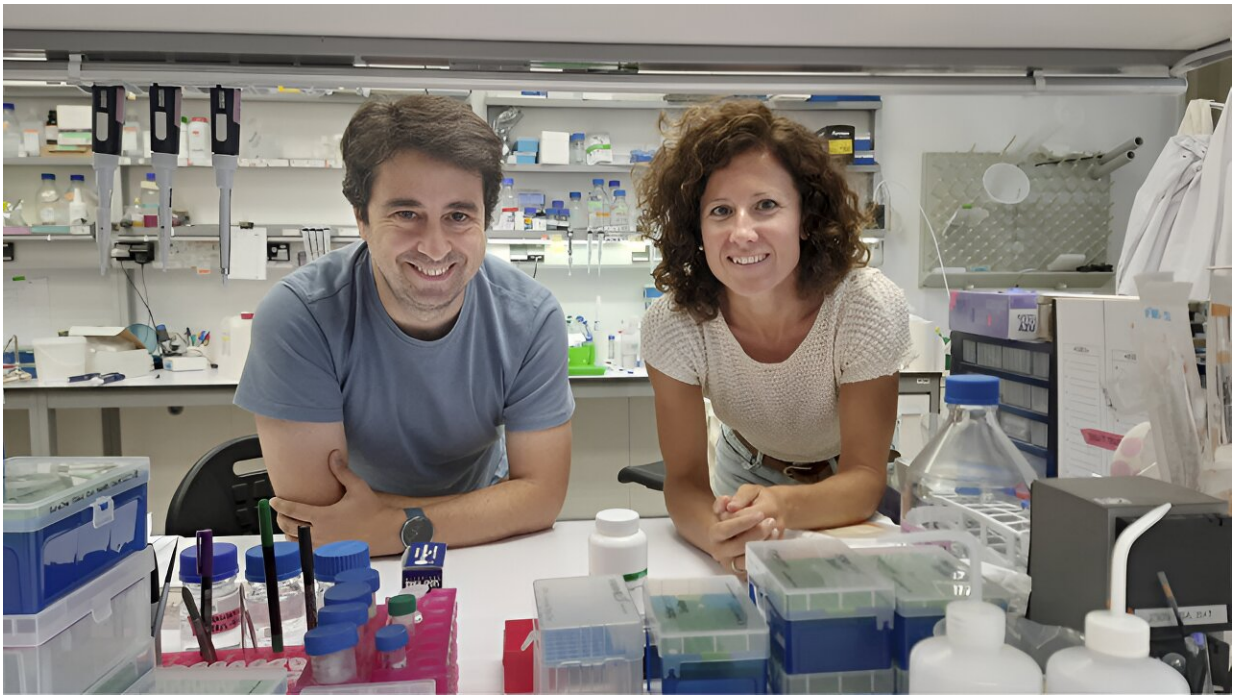

Drs. Albert Quintana and Emma Puighermanal, researchers of the Institut de Neurociències at the Universitat Autònoma de Barcelona. Credit: INc-UAB

A study led by the UAB Institut de Neurociències and published in the journal *Nature Communications* demonstrates in animal models how daily administration of cannabidiol (CBD), a substance obtained from the cannabis plant, extends lifespan and improves symptoms associated with Leigh syndrome.

This severe mitochondrial disease affecting children is characterized by a progressive decline in cognitive and motor functions and premature death. The research group also demonstrated in both mice and fibroblasts from children with the disease that CBD improves cellular function.

Leigh syndrome is a rare mitochondrial disease particularly affecting the organs and tissues that require most energy: the muscles and nervous system. It is characterized by progressive neuromuscular decline and premature death, and there are currently no approved treatments. That is why it is urgent to find a solution for patients suffering from this disease.

Drs. Emma Puighermanal and Albert Quintana, researchers from the Laboratory of Mitochondrial Neuropathology of the Institut de Neurociències at the Universitat Autònoma de Barcelona (INc-UAB), have spent years studying the disease. They seek to understand the processes causing dysfunction of mitochondria, organelles in charge of providing energy to cells, and to find therapies capable of reverting this.

In the study, researchers demonstrated that daily administration of CBD is a promising treatment option. Through its multiple actions, it provides antioxidant, anti-inflammatory and anticonvulsant effects, which improve the symptomatology and help recover cell functions in patients. The study was conducted with two different Leigh syndrome mouse models, as well as with fibroblast cells from patients.

The results revealed that CBD acts at many levels within the cell, including activating a protein inside the cell nucleus known as PPARγ. This protein regulates the expression of many genes involved in the immune response, oxidation and mitochondrial function, and has been seen to be altered by the disease. Moreover, CBD increases the expression of the metallothionein protein, which enhances its antioxidant response.

In the animal models, cannabidiol administration improved neuropathology in the affected brain regions, breathing abnormalities and social deficits, and also delayed motor decline and neurodegenerative signs. In addition, mice receiving treatment lived significantly longer than those with no treatment. In the fibroblast cells from patients, CBD improved their antioxidant processes.

"The benefits we observed, together with CBD's safe and well-tolerated profile, show it to be a truly promising treatment for patients with Leigh syndrome," explains Dr. Albert Quintana, researcher at the INc-UAB and lecturer in the Department of Cellular Biology, Physiology and Immunology at the UAB.

One year ago, the researchers obtained an orphan drug designation for CBD by the European Medicines Agency, which entails many benefits such as a reduction in the costs of developing the drug.

"CBD has already been approved by the US regulatory agency FDA for the treatment of other rare pediatric diseases. We hope all of this will help in the translation of our results to clinical practices," concludes Dr. Emma Puighermanal, researcher at the INc-UAB and lead author of the article.

More information: Emma Puighermanal et al, Cannabidiol ameliorates mitochondrial disease via PPARγ activation in preclinical models, *Nature Communications* (2024). DOI: 10.1038/s41467-024-51884-8

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