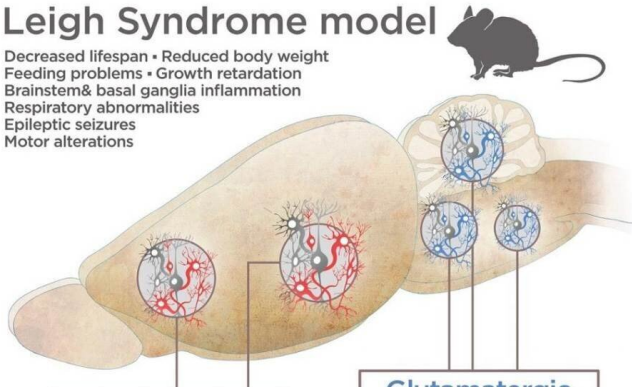


Two groups of neurons identified in causing Leigh syndrome

18 September 2019

Leigh Syndrome model

Decreased lifespan • Reduced body weight
Feeding problems • Growth retardation
Brainstem & basal ganglia inflammation
Respiratory abnormalities
Epileptic seizures
Motor alterations



Leigh syndrome infography. Credit: A. Quintana

Leigh syndrome affects one in every 40,000 newborns and is produced by deficits in the mitochondria, which produce the energy needed for cells to function correctly. Thus, cells with a high energy demand, such as the brain and muscles, are most affected. Recently, the Mitochondrial Neuropathology laboratory at the UAB Institute of Neuroscience, directed by Albert Quintana, published an article in *eLife* describing the neurons responsible for the symptoms produced by this disorder. The generation of two new mouse models of the disease has allowed researchers to better understand the causes.

In order to establish which neurons were responsible for the symptoms, researchers deactivated the *Ndufs4* gene, a key piece of the mitochondria in three types of neurons: the glutamatergic neurons, which activate other [cells](#); the GABAergic neurons, which inhibit other cells; and the [cholinergic neurons](#), which carry information from the brain to the organs. The mice with modified cholinergic neurons did not present any manifestation of the [disease](#), whereas the others did. In both cases, the mice had very low body weight and died prematurely. Therefore, this

is the first time that evidence has been found that the neurons releasing glutamate and GABA are related to Leigh syndrome, while cholinergic neurons are not.

Notable differences were also observed in the two cell types related to the disorder. The mice with symptoms in the activator neurons showed severe problems with breathing and movement, functions related to the brainstem. Those with affected inhibitor neurons, however, presented severe cases of epilepsy, given that the function of these is to prevent brain activities which can lead to this disorder, as well as premature death.

Researchers tested these discoveries at different levels and with the use of various techniques, and the study therefore represents an important step in the direction of finding and developing a treatment.

"One of the greatest unanswered questions about mitochondrial disease is being able to identify why only some neurons are affected by this mutation and what role they play in the development of the disease. In this study we were able to develop new Leigh syndrome models, which has allowed us to name these [neurons](#) and clarify their involvement in the disease," explains Albert Quintana.

To date, no cure has been found for this disease and in the majority of cases, patients die prematurely. With studies like this, researchers can begin to search for specific treatments depending on the type of affected neuron.

More information: Irene Bolea et al. Defined neuronal populations drive fatal phenotype in a mouse model of Leigh syndrome, *eLife* (2019). [DOI: 10.7554/eLife.47163](https://doi.org/10.7554/eLife.47163)

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