



Seminarios internos del IBFG

Dissecting a neuron-to-liver crosstalk to modulate lipid metabolism in Batten disease

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Jueves 11 de Abril de 2019

The magnitude of the neurological diseases burden is huge for patients, families and the public health system. Currently, the research focus aims to understand the delicate homeostasis that controls neural metabolism. The central nervous system (CNS) obtains energy not only from glucose but also from lipids. Moreover, CNS is the major regulator of lipid metabolism hence not surprisingly deregulation of lipid metabolism in neurons is a major contributor of neurological diseases.

Batten disease is the most common of the rare neurodegenerative disorders in children. It is a neurometabolic disorders, which main feature is lysosomal accumulation of insoluble lipid precipitates. Specifically, lysosomes are the only organelles able to catabolise lipids to obtain energy. The autophagic machinery provides lipids to the lysosome in a process termed lipophagy. Although defective autophagy has been related to neurological diseases, the link between Batten disease and lipophagy is unknown.

Our preliminary data shows an impairment of lipophagy in a genetic mouse model of Batten disease. We hypothesize that the disruption of lipophagy in the CNS causes neuronal death, which disrupts lipid metabolism in peripheral tissues. In this project we will determine the mechanism by which lipid metabolism is defective in Batten disease. Moreover, we will ascertain whether uncoupling the liver from CNS rescues lipid metabolism and ameliorates some of the phenotypes related to this disorder. With the expected results we hope to unravel a novel mechanism controlling whole-body lipid homeostasis thus potentially paving the way to find novel therapeutic approaches to treat Batten disease.