Modulators of neuroinflammation have a beneficial effect in Lafora disease

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Progressive myoclonus epilepsy of Lafora type or Lafora Disease (LD; OMIM# 274780) is a rare neurodegenerative disease characterized by generalized epileptic seizures and polyglucosan inclusions, called Lafora bodies (LBs), typically in brain but also in other peripheral tissues such as heart, liver or muscle. LD is a recessive autosomic pathology caused by mutations in two genes *EPM2A* and *EPM2B*, which respectively encode laforin, a dual specificity phosphatase, and malin, a E3-ubiquitin ligase. Both proteins assemble to work as a functional complex which is involved in the regulation of glycogen synthesis and additional physiological pathways. Loss of function of laforin or malin are clinically indistinguishable and have been related with oxidative stress, autophagic impairment, malfunction of cellular proteostasis and neuroinflammation. However, much still remains to be known about the molecular bases of LD and unfortunately an appropriate treatment is missing, therefore patients die within 10 years from the onset of the disease. Using a malin-deficient mouse model (*Epm2b*$^{-/-}$) we are testing different pharmacological approaches in order to assess their efficacy ameliorating the pathological phenotype showed in mice such as polyglucosan inclusions, neurological alterations in brain and neuropsychological decline. With this aim, *Epm2b*$^{-/-}$ mice received treatment with two compounds which the main therapeutic mechanism is to modulate neuroinflammation. Next, we performed a battery of behavioral tests and histopathological analysis to evaluate whether modulating neuroinflammation has a therapeutic effectiveness in LD. On the whole, this work shows a preclinical study of modulators of neuroinflammation in *Epm2b*$^{-/-}$ mice as a novel pharmacological strategy in LD.