
Poster

PLA2G6-ASSOCIATED NEURODEGENERATION (PLAN): CHARACTERIZATION OF PATIENTS AND DRUG SCREENING.



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ABSTRACT

Neurodegeneration with brain iron accumulation (NBIA) involve a group of rare neurodegenerative disorders characterized by brain iron accumulation, progressive extrapyramidal dysfunction (dystonia, stiffness, choreoathetosis), and presence of axonal spheroids, usually limited by the central nervous system.

Within the different subtypes of NBIA, in this study we focussed in PLA2G6-associated neurodegeneration (PLAN), diseases caused by a mutation in the phospholipase A2 group VI (PLA2G6). PLA2G6 encodes the enzyme iPLA2b, a calcium-independent phospholipase A2 which is involved in lipid metabolism. The loss of iPLA2b's function result in mitochondrial abnormalities and synaptic transmission impairment in neurons among other alterations.

In the current work we studied the pathophysiology of three confirmed cases of PLAN using fibroblasts derived from the patients: PLAN 10 (heterozygous mutation), PLAN 11(heterozygous mutation) and PLAN 8 (homozygous mutation). The aim of this study is to characterize, in patient-derived fibroblasts, the pathological alterations produced by PLA2G6 mutations. Main methods used were Western blot and Prussian Blue Staining. Our results confirm iron accumulation in patients-derived fibroblasts, impaired autophagy and ferritinophagy, especially in the patient that suffers the homozygous mutation (Plan 8). The purpose is to carry out a drug screening able to reverse the pathophysiology observed.

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