Dysregulation of PLA2G6 activity induces degeneration in astrocytes in culture

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**Introduction**

PLA2G6 activity dysfunction causes neurotrophic degeneration with iron accumulation, which during childhood is lethal, and in adulthood may induce Parkinsonian-like disease (1). Recently, it was shown that fibroblasts from idiopathic or sporadic Parkinson’s disease patients show impaired store-operated calcium entry (SOCE) (2). SOCE controls the activity of Calmodulin, a putative negative regulator of PLA2G6, so the impairment of intracellular calcium flux suggests a role for PLA2G6 in the PD pathology. Here we test the hypothesis that unbalanced activity of PLA2G6 in astrocytes induces deleterious effects on human dopaminergic cells because of their failure to respond with pro-survival/anti-inflammatory signaling to prevent dopaminergic neuronal death and microglia activation.

**Results**

**A** Normal Dopa neurons **B** A-Syn A53T Dopa neurons

**Methods**

**Immunostaining**

Fluorochrome

Secondary Antibody

Primary Antibody

GFAP

Cell Membrane

Nucleus

DAPI

Confocal Microscopy

**Morphological Analysis**

**Statistical Analysis**

**Imaris**

**Imaging & Analysis techniques in Imaris**

**Conclusions**

- PLA2G6 dysfunction affects the production of lipid mediators such as RvD1, RvD5, and Maresin 1
- A53T mutated α-synuclein causes activation of astrocytes to the pro-inflammatory pathway
- PLA2G6 induces changes in morphology of astrocytes resembling the activation into pro-inflammatory phenotype

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