

# C19orf12 Ablation-Caused Iron Accumulation, Mitochondrial Dysfunction, and Susceptibility to Ferroptosis

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Mitochondrial membrane protein associated neurodegeneration (MPAN) is a subtype of a group of rare neurological disorders termed Neurodegeneration with Brain Iron Accumulation (NBIA). MPAN is caused by genetic mutations in the C19orf12 gene in an autosomal recessive manner and it is believed that these mutations cause loss of C19orf12 function. It is characterized by massive iron accumulation and neurodegeneration in the brain. In this study, we aimed to understand how loss of C19orf12 function cause MPAN by investigating C19orf12 KO M17 neuroblastoma cells as a cell model for MPAN. The C19orf12 KO M17 cells demonstrated mitochondria fragmentation and dysfunction, as well as iron accumulation and oxidative stress. The C19orf12 KO cells were also more susceptible to erastin-induced ferroptosis. Pretreatment of DFO, an iron chelator, rescued mitochondrial defects and oxidative stress, and almost completely prevented erastin-induced ferroptosis in the C19orf12 KO M17 cells. These results overall support the notion that C19orf12 ablation-induced iron overload and ferroptosis are critical in the pathogenesis of MPAN.

## Awards Won:

Fourth Award of \$500