

## EFFECT OF OPA1 MUTATIONS ON MITOCHONDRIAL DYSFUNCTION

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Optic atrophy type 1(*OPA1*) is a nuclear dynamin-related GTPase, targeted to the inner mitochondrial membrane, which plays a role in mitochondrial fusion. Mutations in the *OPA1* gene on chromosome 3q28-qter are associated with autosomal dominant optic atrophy (ADOA), the most common inherited optic neuropathy, in which retinal ganglion cells (RGCs) are lost and visual acuity is impaired from an early age. To understand the effects of *OPA1* gene mutations on the mitochondrial function, the lymphocytes obtained from the affected ADOA individuals, non-affected ADOA family were collected and established cell lines. Two ADOA families were enrolled in this study, one is ADOA family I with *OPA1* exon 10 deletion and another is ADOA family II with the deletion in exon 12. In the assessment of *OPA1* mRNA levels and *OPA1* protein profile, the ADOA shows reduced *OPA1* expression depends on individuals with different mutations. The dissipation of mitochondrial membrane potential and a drop of ATP synthesis were evident in lymphocyte cultures carrying pathogenic *OPA1* mutations. In addition, a decrease in mitochondrial mass and mitochondrial DNA copy number and enhanced oxidative damages were also demonstrated. Moreover, confocal microscope revealed increase mitochondrial fragmentation in the lymphocytes from ADOA patients. These findings indicated that *OPA1* plays an important role in the mitochondrial bioenergetics and mitochondrial networks. The change in mitochondrial shape and mitochondrial bioenergetics may be affected of *OPA1* mutations and a cause of disease.

### Key words:

Optic atrophy type 1 (*OPA1*), autosomal dominant optic atrophy, mitochondrial fusion, mitochondrial function