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# Mutation of OPA1 causes dominant optic atrophy with external ophthalmoplegia, ataxia, deafness and multiple mitochondrial DNA deletions: a novel disorder of mtDNA maintenance

Submitted by Emmanuel Lemoine on Wed, 12/11/2013 - 17:08

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| Titre | Mutation of OPA1 causes dominant optic atrophy with external ophthalmoplegia, ataxia, deafness and multiple mitochondrial DNA deletions: a novel disorder of mtDNA maintenance |
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| Auteur | Hudson, Gavin [1], Amati-Bonneau, Patrizia [2], Blakely, Emma L [3], Stewart, Joanna D. [4], He, Langping [5], Schaefer, Andrew M [6], Griffiths, Philip G. [7], Ahlqvist, Kati [8], Suomalainen, Anu [9], Reynier, Pascal [10], McFarland, Robert [11], Turnbull, Douglass M. [12], Chinnery, Patrick F [13], Taylor, Robert W. [14] |
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| Résumé en anglais | Mutations in nuclear genes involved in mitochondrial DNA (mtDNA) maintenance cause a wide range of clinical phenotypes associated with the secondary accumulation of multiple mtDNA deletions in affected tissues. The majority of families with autosomal dominant progressive external ophthalmoplegia (PEO) harbour mutations in genes encoding one of three well-characterized proteins—polγ, Twinkle or Ant 1. Here we show that a heterozygous mis-sense mutation in OPA1 leads to multiple mtDNA deletions in skeletal muscle and a mosaic defect of cytochrome c oxidase (COX). The disorder presented with visual failure and optic atrophy in childhood, followed by PEO, ataxia, deafness and a sensory-motor neuropathy in adult life. COX-deficient skeletal muscle fibres contained supra-threshold levels of multiple mtDNA deletions, and genetic linkage, sequencing and expression analysis excluded POLG1, PEO1 and SLC25A4, the gene encoding Ant 1, as the cause. This demonstrates the importance of OPA1 in mtDNA maintenance, and implicates OPA1 in diseases associated with secondary defects of mtDNA. |
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| DOI | 10.1093/brain/awm272 [20] |
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| Titre abrégé | Mutation of OPA1 causes dominant optic atrophy with external ophthalmoplegia, ataxia, deafness and multiple mitochondrial DNA deletions |

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**Liens**
[1] http://okina.univ-angers.fr/publications?f[author]=886
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