

# Haploinsufficiency due to a novel *ACO2* deletion causes mitochondrial dysfunction in fibroblasts from a patient with dominant optic nerve atrophy

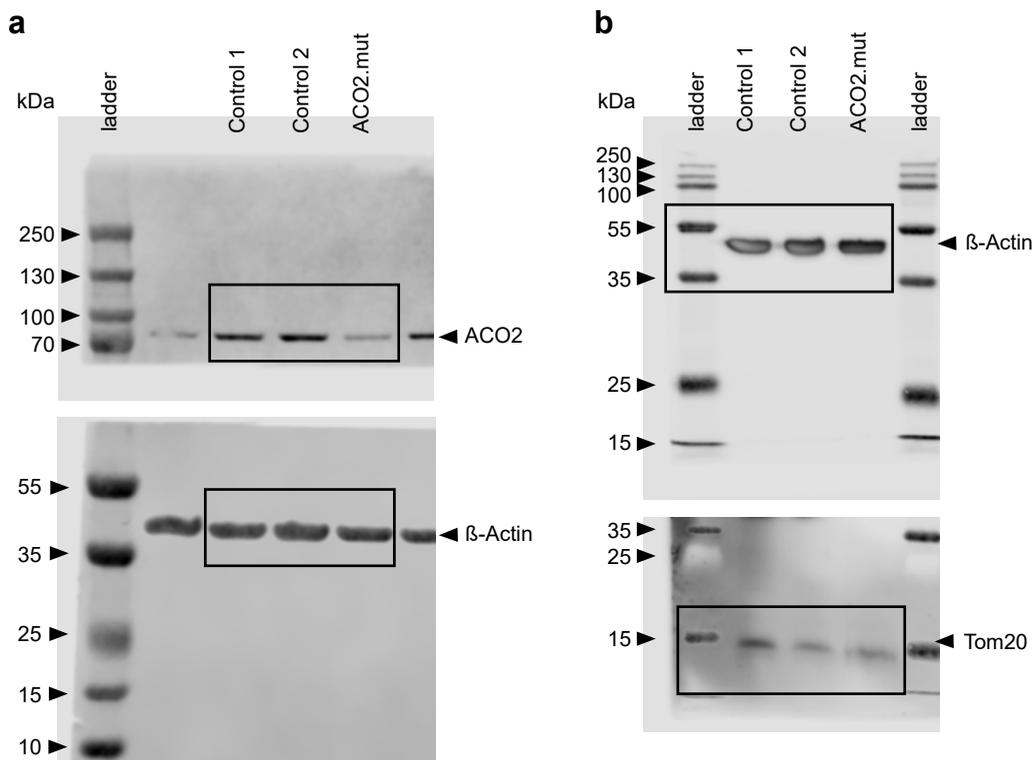
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Supplementary Figure 1:

Identity:	514/784 (65.6%)	
Similarity:	618/784 (78.8%)	
NP_001089.1	1 MAPYSLLVTR--LQKALGVRQYHVASVLCQRAKAVAMSHFEPNEYIHYDLL	48
NP_013407.1	1 ----MLSARSAIKRPI-VRGLATVSNLTRDSKVNQNLLEDHSFINYKQN	44
NP_001089.1	49 EKNINIVRKRRLNRPLTLSEKIVYGHLDPPASQEIERGKSYLRLRPDRVAM	98
NP_013407.1	45 VETLDIVRKRRLNRPFYAEKILYGHLDPPHGQDIQRGVSYLKLRPDRVAC	94
NP_001089.1	99 QDA AQMAMLQFISSGLSKVAVPSTIH DH IEAQVGG EKDLRRAKIDNQ	148
NP_013407.1	95 QDATAQMAILQFMSAGLPQVAKPVTVHCDHLIQAQVGG EKDLKRAIDLNK	144
NP_001089.1	149 EYVNF L ATAGAKYGVGFWKPGSGIIHQIILENYAYPGVLLIG DSH PNG	198
NP_013407.1	145 EYVDF LASATAKYNMGFWKPGSGIIHQIVLENYAFPGALIIIGTDSHTPNA	194
NP_001089.1	199 GGLGGICIGVGGADAVDMAGIPWELKCKPKVIGVKLTGSLSGWSSPKDVI	248
NP_013407.1	195 GGLGQLAIGVGGADAVDMAGRPELWELKAPKILGVKLTGKMNGWTSPKDII	244
NP_001089.1	249 LKVAGILTVKGGTGAIVEYHGPVDSISCTGMATIN GAEIGATTSVFP	298
NP_013407.1	245 LKLAGITTVKGGTGKIVEYFGDGVDTFSATGMGTCINMGAEIGATTSVFP	294
NP_001089.1	299 YNHRMKKYL SKTGREDIANLADEF -KDHLVPDPGCHYDQLIEINLSELKP	347
NP_013407.1	295 FNKSMIEYLEATGRGKIADFAKLYHKDLLSADKDAEYDEVVEIDLNTLEP	344
NP_001089.1	348 HINGPFTPDLAHPVAEVGKVAEKEGWPLDIRVGLIGSCTNSSYEDMGRSA	397
NP_013407.1	345 YINGPFTPDLATPVSKMKEVAVANNWPLDVRVGLIGSCTNSSYEDMGRSA	394
NP_001089.1	398 AVAKQALAHGLKCKSQFTITPGSEQIRATI ERDGYAQILRDLGGIVLANA	447
NP_013407.1	395 SIVKDAAAHGLKSKTIFTVTPGSEQIRATI ERDGLQLETFKEFGGIVLANA	444
NP_001089.1	448 CGICIGQWDRDKIKKGEKNTIVTS YNRIFTRLDANPETHAFVTSPEIVT	497
NP_013407.1	445 CGPICIGQWDRDIIKKGDKNTIVSSYRNFTSRNDGNPQTHAFVASPELVT	494
NP_001089.1	498 ALAIAGTLKFNPETDYLTGTDGKKFRLEAPDADELPGKEFDPGQDQYQHP	547
NP_013407.1	495 AFAIAGDLRFNPLTDKLDKDGNEFMLKPPHGDGLPQRGYDAGENTYQAP	544
NP_001089.1	548 PKDSSGQHVDVSPTSQRLLLEPFDKWDGKLEDLQLIKVKGKCTTDHI	597
NP_013407.1	545 PDRSTVEVKVSPSDRLQLLKPFPKWDGKDAKDMPILIKAVGKTTTDHI	594
NP_001089.1	598 SAAGPWLKFRGHLDNISNLLIGAINIENKANSVRNAVTFEGVPVPTA	647
NP_013407.1	595 SMAGPWLKYRGHLENISNNYMIGAINAENKANCNVVYTYEYKVPVPTA	644
NP_001089.1	648 RYYKKGIRWVIGDENYEGSSREHAAL EPHLGGRAIITKSFARIHET	697
NP_013407.1	645 RDYRDQGIKVVIGDENFEGSSREHAAL EPRFLGGFAIITKSFARIHET	694
NP_001089.1	698 NLKKQGLLPLTFADPADYNKIHPVDKLTIQGLKDFTPGKPLKCIKHPNG	747
NP_013407.1	695 NLKKQGLLPLNFKNPADYDKINPDDRIDLGLAELAPGKPVMTMRVHPKNG	744
NP_001089.1	748 TQETILLNHTFNETQIEWFRAGSALNRMKELQQ- 780	
NP_013407.1	745 KPWDAVLTHTFNDEQIEWFKYGSALNKIKAEDEK 778	

Multiple sequence alignment of human *ACO2* (NP\_001089.1) and yeast *ACO1* (NP\_013407.1) generated by MUSCLE version 3.6 using the option maxiters 2 [Edgar, R.C. MUSCLE: multiple sequence alignment with high accuracy and high throughput. *Nucleic Acids Res.* 32, 1792-7 (2004)]. Residues interacting with the substrate are highlighted in green [Lauble, H. et al., Crystal structures of aconitase with isocitrate and nitrocitrate bound. *Biochemistry* 31, 2735-48 (1992)]. The deletion site is highlighted in red.

Supplementary Figure 2:



a) Image of Western blot membranes for fibroblast samples Control 1, Control 2 and ACO2.mut probed with antibodies against ACO2 and  $\beta$ -Actin. Black boxes indicate the image sections shown in Figure 3A. b) Image of Western blot membranes of fibroblast samples Control 1, Control 2 and ACO2.mut were probed with antibodies against  $\beta$ -Actin and Tom20. Black boxes indicate the image sections shown in Figure 3C. Bands of the protein ladder are indicated on the right or the left side of the images. The size of the protein ladder bands are indicated in kDa and black arrow heads. The identity of the samples is indicated at the top of each membrane.