

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

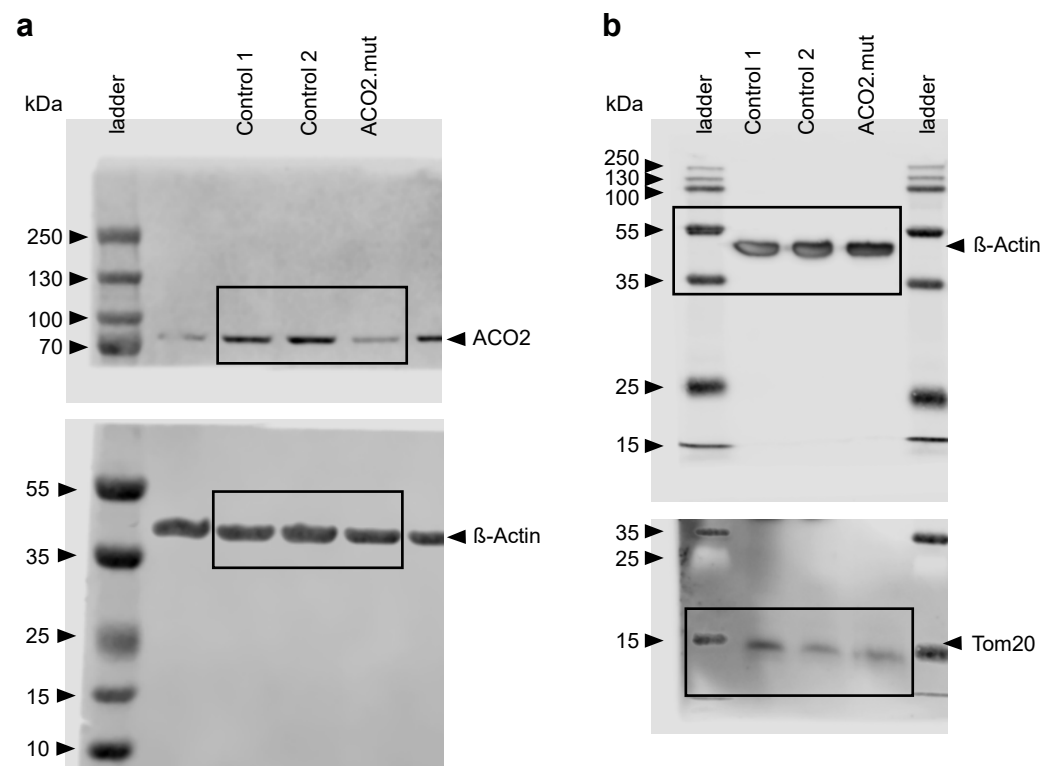
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Supplementary Figure 1:

Identity:	514/784 (65.6%)	
Similarity:	618/784 (78.8%)	
NP_001089.1	1 MAPYSLLVTR--LQKALGVRQYHVASVLCQRAKVAMSHFEPNEYIHYDLL	48
NP_013407.1	1 ----MLSARSAIKRPI-VRGLATVSNLTRDSKVNQNLLEDHSFINYKQN	44
NP_001089.1	49 EKNINIVRKRLNRPLTLSEKIVYGHLD DPASQEIERGKSYLRLRPDRVAM	98
NP_013407.1	45 VETLDIVRKRLNRPFYAEKILYGHLD DPHGQDIQRGVSYLKLRPDRVAC	94
NP_001089.1	99 QDA AQMAMLQFISSGLSKVAVPSTIH DH IEAQVGGEKDLRRAKDINQ	148
NP_013407.1	95 QDATAQMAILQFMSAGLPQVAKPVTVHCDHLIQAQVGGEKDLKRAIDLNK	144
NP_001089.1	149 EVYNFLATAGAKYGVGFWKPGSGIIHQIILENYAYPGVLLIG DSH PNG	198
NP_013407.1	145 EVYDFLASATAKYNMFGWKPGSGIIHQIVLENYAFPGALIIIGTDSHTPNA	194
NP_001089.1	199 GGLGGICIGVGGAADVDMAGIPWELKCPKIVGVKLTGSLSGWSSPKDVI	248
NP_013407.1	195 GGLGQLAIGVGGAADVDMAGRPWELKAPKILGVKLTGKMNGWTSPKDII	244
NP_001089.1	249 LKVAGILTVKGGTGAIVEYHGPVDSISCTGMATINNGAEIGATTSVFP	298
NP_013407.1	245 LKLAGITTVKGGTGKIVEYFGDGVDTFSATGMGTICNMGAEIGATTSVFP	294
NP_001089.1	299 YNHRMKYLSKTGREDIANLADEF-KDHLVPDPGCHYDQLIEINLSELKP	347
NP_013407.1	295 FNKSMIEYLEATGRGKIADFAKLYHKDLLSADKDAEYDEVVEIDLNTLEP	344
NP_001089.1	348 HINGPFTPDLAHPVAEVGKVAEKEGWPLDIRVGLIGSCN SSYEDMGRSA	397
NP_013407.1	345 YINGPFTPDLATPYSKMKEVAVANNWPLDVRVGLIGSCTN SSYEDMGRSA	394
NP_001089.1	398 AVAKQALAHGLKCKSQFTITPGSEQIRATIERDGYAQILRDLGGIVLANA	447
NP_013407.1	395 SIVKDAAAHGLKSKTIFTVTPGSEQIRATIERDGLQLETFKEFGGIVLANA	444
NP_001089.1	448 CGICIGQWDRDKIKKGEKNTIVTS NRI FTGR DANPETHAFVTSPEIVT	497
NP_013407.1	445 CGPCIGQWDRRIDKKGDKNTIVSSYNRNFTSRNDGNPQTHAFVASPELVT	494
NP_001089.1	498 ALAIAGTLKFNPETDYLTTGTDGKKFRLEAPDADELPKGEFDPGQDQYQHP	547
NP_013407.1	495 AFAIAGDLRFNPLTDKLDKDGNEFMLKPPHGDGLPQRGYDAGENTYQAP	544
NP_001089.1	548 PKDSSGQHVDVSPTSQRLLLEPFDKWDGKDLEDLQ LIKVGKCTTDHI	597
NP_013407.1	545 PADRSTVEVKVSPTSDDLQLLKPFPKWDGKDAKDMPILIKAVGKTTTDHI	594
NP_001089.1	598 SAAGPWLKFRGHLDNISNNLLIGAINIENGKANSVRNAVTFEGVPVPTA	647
NP_013407.1	595 SMAGPWLKYRGHLENISNNYMIGAINAENKANCVKNVYTGEYKGVPTA	644
NP_001089.1	648 RYYKKHGIRWVIGDENYEGGSSREHAALEPHRLGGRAITKSFARIHET	697
NP_013407.1	645 RDYRDQGIKWVIGDENFEGGSSREHAALEPRFLGGFAITKSFARIHET	694
NP_001089.1	698 NLKKQGLLPLTFADPADYNKIHPVDKLTIQGLKDFTPGPKLKCIHKPNQ	747
NP_013407.1	695 NLKKQGLLPLNFKNPADYDKINPDDRIDI LGLAELAPGKPVMTMRVHPKNG	744
NP_001089.1	748 TQETILLNHTFNETQIEWFRAGSALNRMKELQQ- 780	
NP_013407.1	745 KPWDAVLTHTFNDEQIEWFKYGSALNRIKADEKK 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 β-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 β-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.