# Supplementary information

# Lipid storage myopathy associated with sertraline treatment is an acquired mitochondrial disorder with respiratory chain deficiency

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#### **Material and Methods**

Patient	Acylcarnitines, free carnitine (C0)	U-organic acids	Lactic acid (serum) (0,5-1,7 mmol/L)
1	Increased C12, C14, C16, C18, and C18:1, slightly reduced C0 (20 days after biopsy)	No pathological excretion	<ul> <li>1.9 (3 month after biopsy)</li> <li>1.4 (14 month after biopsy)</li> <li>1.5 (16 month after biopsy)</li> <li>2.0 (3 years after biopsy)</li> <li>2.2 (7 years after biopsy)</li> </ul>
2	Increased C6, C8, C10, C12, C14, C16, C14:1, C18:1 and C18 (25 days after biopsy)		<b>3.2</b> (3 month after biopsy)
3	Carnitine deficiency with low concentration of C0 and total carnitines (same day as biopsy)		
4	Increased C4, C6, C10, C12, C14, C16, C14:1, C18:1 and C18, slightly reduced C0 (30 days after biopsy)	Increased excretion of ethylmalonic acid (EMA) and 2-hydroxyglutaric acid (2- HGA) (35 days after biopsy)	1.3 (4 month after biopsy)
5	Increased C6, C8, C10 and C12 (1 month after biopsy) Increased C4, C6, C8, C10, C12, C14 and C14:1 (2 month after biopsy)		
6	Increased C4, C6, C10, C12, C14, C16, C14:1, C18:1 and C18 (7 days before biopsy)	Increased excretion of EMA and 2-HGA, adipic acids and isovaleryglycine (7 days before biopsy)	
7	Carnitine deficiency with low concentration of C0 and total carnitines (3 days after biopsy)	No patological excretion (23 days after biopsy)	
8	Increased C6, C8, C10, C12, C14, C16, C14:1, C14:2, C18:1, C18 and C5DC (8 month after biopsy)		
9	Increased C12 (1.5 month after biopsy), Increased C12, C14 and C14:1 (6 month after biopsy)	No pathological excretion (6 month after biopsy)	1.2 (6 month after biopsy)
10	Increased C6, C8, C10, C12, C14, C16, C14:1, C18:1 (4 month after biopsy)	No pathological excretion (4 month after biopsy)	1.2 (4 month after biopsy)
11	Increased C4, C5, C6, C8, C10, C12, C14, C16, C14:1, C14:2, C18:1, C18 and C5DC (1.5 month after biopsy)	No pathological excretion (1,5 month after biopsy)	<b>3.1</b> (1.5 month after biopsy)

Supplementary Table 1. Detailed laboratory findings in all patients

Method	Muscle biopsy findings	Age at biopys (Y)	Sex
Western blot			
DC1	Muscle biopsy with lipid storage (MADD, <i>ETFDH</i> )	25	М
DC2	Muscle biopsy with lipid storage (Neutral lipid storage disease with myopathy, <i>PNPLA2</i> )	43	F
C1	Normal muscle biopsy	22	М
C2	Normal muscle biopsy	45	F
C3	Normal muscle biopsy	58	F
Proteomic profiling			
C1	Normal muscle biopsy	52	М
C2	Same as C1 in western blot	22	М
C3	Normal muscle biopsy	61	М
C4	Normal muscle biopsy	48	М
C5	Same as C2 in western blot	45	F
C6	Normal muscle biopsy	43	F
C7	Normal muscle biopsy	26	F
C8	Same as C3 in western blot	58	F

#### Supplementary Table 2. A summary of controls used in this study

Y, year; F, female; M, Male; DC, disease control; C, control (from individuals who had been investigated for a possible muscle disorder, but in whom investigations excluded muscle disease)

#### Immunofluorescence analysis of respiratory chain Complexes I, II and IV

Cryosections from each patient were divided into two separate staining sets: one set included complexes I, II, VDAC1, and perlecan and the other set included complexes I, IV, VDAC1, and perlecan. The sections were fixed in 4% formaldehyde in 0.1 M phosphate buffer for 10 minutes at 4°C, then rinsed with water three times and washed in Tris-buffered saline with Tween 20 (TBS-T) for 10 minutes. Permeabilisation was carried out through a graded methanol series (70% 2 minutes, 95% 2 minutes, 100% 10 minutes, 95% 2 minutes, and 70% 2 minutes), followed by another wash in TBS-T for 5 minutes. The sections were subsequently processed using a Dako Autostainer, where the sections were blocked with 10% normal goat serum before incubating with the primary antibodies and the corresponding fluorochrome-conjugated secondary antibodies (Supplementary Table 2).

All slides were scanned using a Hamamatsu S60 digital scanner with fluorescence equipment, including a DAPI/FITC/TRITC/Cy5 quad-band filter set (Semrock, New York). Results from studies using this assay on biochemically and genetically verified cases with isolated Complex I and IV deficiency and well characterized and genetically defined patients with combined complex I and IV deficiency are shown in Supplementary Fig 1.

Antigen	Host	Host Dilution			Manufacturer	
(Isotype/Conjugation)		MIFA	MITIF	WB	(Catalogue Number)	
		Primary	antibodies			
NDUFB8 (Complex I)	Mouse		1:200	1:1000	Abcam (ab110242)	
(IgG1)						
SDHB (Complex II)	Mouse		1:200	1:1000	Abcam (ab14714)	
(IgG2a)						
UQCRC2 (Complex III)	Mouse			1:2000	Abcam (ab14745)	
(IgG1)						
MTCO1 (Complex IV)	Mouse		1:200	1:1000	Abcam (ab14705)	
(IgG2a)						
ATPB (Complex V)	Mouse			1:2000	Abcam (ab14730)	
_(IgG1)						
VDAC1 (Porin)	Mouse		1:1000		Abcam (ab14734)	
(IgG2b)						
VDAC1	Rabbit			1:1000	Cell Signaling Technology	
(IgG)					(4661)	
MYH7 (MyHC I)	Mouse	1:50			DSHB (BA-D5)	
(IgG2b)						
MYH2 (MyHC IIa)	Mouse	1:50			DSHB (SC-71)	
(IgG1)						
MYH1 (MyHC IIx)	Mouse	1:10			DSHB (6H1)	
(IgM)						
Heparan Sulfate	Rat	1:200	1:1000		Merck (MAB1948P)	
Proteoglycan (Perlecan)						
(IgG2aк)						

Supplementary Table 3. A	ntibodies for immunofluc	prescence and western blot analyses
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	Secondary antibodies						
Mouse IgG (HRP)	Goat			1:1000	ThermoFisher Scientific (32430)		
Rabbit IgG (HRP)	Goat			1:1000	ThermoFisher Scientific (32460)		
Mouse IgG1 (Alexa Fluor 488)	Goat	1:200	1:200		ThermoFisher Scientific (A-21121)		
Mouse IgM (H) (Alexa Fluor 647)	Goat	1:200			ThermoFisher Scientific (A-21238)		
Mouse IgG2a (Alexa Fluor 647)	Goat		1:100		ThermoFisher Scientific (A-21241)		
Mouse IgG2b (Brilliant Violet 421)	Goat	1:200	1:100		Jackson ImmunoResearch (115-675-207)		
Rat IgG (H+L) (Alexa Fluor 568)	Goat	1:200	1:250		ThermoFisher Scientific (A-11077)		

HRP: Horseradish peroxidase



# Isolated Complex I deficiency



# Isolated Complex IV deficiency





**Supplementary Fig 1.** Quadruple immunofluorescence assay applied on well characterized diseases and normal muscle. In merged illustrations yellow fibers are normal, red fibers are Complex I deficient, green fibers are Complex IV deficient and blue fibers are deficient of both Complex I and IV.

a-d) Normal muscle. e-h) Patient with isolated Complex I deficiency (Darin et al. Eur J Neurol. 2017;24:587-93). i-l) Patient with isolated Complex IV analysis (Roos et al. Eur J Hum Genet. 2019;27:331-5). m) mtDNA variant m.3243A>G associated with mitochondrial encephalomyopathy lactic acidosis and stroke-like periods (MELAS). n) Single large scale mtDNA deletion o) Multiple large and small deletions in inclusion body myositis (IBM). p) Normal control. Bars = 50 μm.

#### Proteomic Liquid Chromatography-Mass Spectrometry (LC-MS<sup>3</sup>) analysis

#### Sample preparation

Proteins were extracted in 2% sodium dodecyl sulfate and 100 mM triethylammonium bicarbonate (TEAB) using a Covaris ML230 ultrasonicator. Protein concentrations were determined using Pierce BCA Protein Assay Kit (Thermo Scientific) on a SpectraMax iD3 microplate reader (Molecular Devices). Samples (40 µg) were processed using a modified SP3 method. Samples were reduced in 10mM dithiothreitol at 56°C for 30min and alkylated in 20mM iodoacetamide at room temperature for 30min. Washed hydrophobic and hydrophilic Sera-Mag<sup>™</sup> SpeedBeads (Carboxylate-Modified, by Cytiva) were added to the samples with a bead to protein ratio of 18:1. Proteins were precipitated on the beads by ethanol (final concentration 70%), washed twice with 70% ethanol, followed by wash with 100% acetonitrile, dried at room temperature. Beads were resuspended in 50mM TEAB and proteins were digested with Trypsin/Lys-C mix (1:25, Promega) for two hours, followed by trypsin (1:50, Promega) overnight. The magnetic beads were removed, and samples were labelled using TMTpro 18-plex isobaric mass tagging reagents (Ref#: A52045; Lot#: XI346567 and XJ346678, Thermo Fisher Scientific). The labelled samples were pooled and purified using HiPPR Detergent Removal Resin and Pierce peptide desalting spin columns (both Thermo Scientific), according to the manufacturer's instructions. The TMT-set was fractionated by basic reversed-phase chromatography on a Dionex Ultimate 3000 UPLC system (Thermo Fisher Scientific). Peptide separations were performed using a reversed-phase XBridge BEH C18 column (3.5 µm, 2.1x250 mm, Waters Corporation) and a stepped gradient from 3% to 80% solvent B over 90 min at a flow of 200 µL/min. Solvent A was 25mM ammonia and solvent B was 85% acetonitrile. Fractions (96) were collected from 20-74 minutes and combined into 36 final fractions. Fractions were evaporated and reconstituted in 3% acetonitrile, 0.1% trifluoroacetic and 0.015% dodecyl-β-D-maltoside for LC-MS<sup>3</sup> analysis.

#### LC-MS<sup>3</sup> analysis

The fractions were analysed on an Orbitrap Lumos<sup>™</sup> Tribrid<sup>™</sup> mass spectrometer equipped with a FAIMS Pro ion mobility system and interfaced with an Easy-nLC1200 liquid chromatography system (all Thermo Fisher Scientific). Peptides were trapped on an Acclaim Pepmap 100 C18 trap column (100 µm x 2 cm, particle size 5 µm, Thermo Fisher Scientific) and separated on an in-house packed analytical column (35 cm x 75 µm, particle size 3 µm, Reprosil-Pur C18, Dr. Maisch) using a stepped gradient from 5% to 35% B over 77 min at a flow of 300 nL/min (Solvent A 0.2% formic acid, solvent B 80% ACN and 0.2% formic acid). FAIMS Pro was alternating between the compensation voltages (CV) of -50 and -70, and the same data-dependent settings were used at both CVs. The precursor ion mass spectra were acquired at a resolution of 120 000 and an m/z range of 375-1375. Using a cycle time of 1.5 seconds the most abundant precursors with charges 2–7 were isolated with an m/z window of 0.7 and fragmented by collision-induced dissociation (CID) at 35%. Fragment spectra were recorded in the ion trap at a Rapid scan rate. Dynamic exclusion was set to 60 sec. The ten most abundant MS2 fragment ions were isolated using multi-notch isolation for further MS<sup>3</sup> fragmentation. MS<sup>3</sup> fragmentation was performed using higher-energy collision dissociation (HCD) at 55% and the MS<sup>3</sup> spectra were recorded in the Orbitrap at 50 000 resolution and an m/z range of 100–500.

#### Proteomic data analysis

Raw files were processed and analyzed with Proteome Discoverer (ver 3.0, Thermo Fisher Scientific) The data was matched against *Human* SwissProt database (20597 entries, February 2024) using Sequest as a search engine

with a precursor tolerance of 5 ppm and a fragment ion tolerance of 0.6 Da. Tryptic peptides were accepted with 1 missed cleavage. Methionine oxidation and acetylation on protein N-termini was set as variable modifications and cysteine carbamidomethylation, TMTpro on lysine and peptide N-termini were set as fixed modifications. Percolator was used for PSM validation with a strict FDR threshold of 1%. For quantification TMT reporter ions were identified in the MS<sup>3</sup> HCD spectra with 3 mmu mass tolerance and the TMT reporter intensity values for each sample were normalized on the total peptide amount. The SPS threshold was set to 65%, a Sequest HT threshold score of 2 was chosen. Only unique peptides were used for relative quantification and proteins were required to pass a protein FDR of 1%.

#### Quantitative LC-MS<sup>3</sup> proteomic analysis and illustration by volcano plots

For quantitative LC-MS<sup>3</sup> proteomic analysis and illustration by volcano plots of the respiratory chain Complex I-V, the beta-oxidation of fatty acids (FAO) and the citric acid cycle (TCA), genes were selected based on "MitoCarta3.0: An Inventory of Mammalian Mitochondrial Proteins and Pathways" (https://www.broadinstitute.org/mitocarta/mitocarta30-inventory-mammalian-mitochondrial-proteins-andpathways).

#### **Complex I**

#### CI subunits

MT-ND1, MT-ND2, MT-ND3, MT-ND4, MT-ND4L, MT-ND5, MT-ND6, NDUFA1, NDUFA10, NDUFA11, NDUFA12, NDUFA13, NDUFA2, NDUFA3, NDUFA5, NDUFA6, NDUFA7, NDUFA8, NDUFA9, NDUFAB1, NDUFB1, NDUFB10, NDUFB11, NDUFB2, NDUFB3, NDUFB4, NDUFB5, NDUFB6, NDUFB7, NDUFB8, NDUFB9, NDUFC1, NDUFC2, NDUFS1, NDUFS2, NDUFS3, NDUFS4, NDUFS5, NDUFS6, NDUFS7, NDUFS8, NDUFS8, NDUFV1, NDUFV2, NDUFV3

#### CI assembly factors

ACAD9, AIFM1, COA1, DMAC1, DMAC2, ECSIT, FOXRED1, LYRM2, NDUFAF1, NDUFAF2, NDUFAF3, NDUFAF4, NDUFAF5, NDUFAF6, NDUFAF7, NDUFAF8, NUBPL, TIMMDC1, TMEM126A, TMEM126B, TMEM186, TMEM70

Complex II <u>CII subunits</u> SDHA, SDHB, SDHC, SDHD

<u>CII assembly factors</u> SDHAF1, SDHAF2, SDHAF4, SDHAF3

### **Complex III**

<u>CIII subunits</u> CYC1, MT-CYB, UQCR10, UQCR11, UQCRB, UQCRC1, UQCRC2, UQCRFS1, UQCRH, UQCRQ

# CIII assembly factors

BCS1L, LYRM7, TTC19, UQCC1, UQCC2, UQCC3

# **Complex IV**

# CIV subunits

COX4I1, COX4I2, COX5A, COX5B, COX6A1, COX6A2, COX6B1, COX6B2, COX6C, COX7A1, COX7A2, COX7A2L, COX7B, COX7B2, COX7C, COX8A, COX8C, MT-CO1, MT-CO2, MT-CO3, NDUFA4

# CIV assembly factors

CEP89, CMC1, CMC2, COA1, COA3, COA4, COA5, COA6, COA7, COA8, COX10, COX11, COX14, COX15, COX16, COX17, COX18, COX19, COX20, HIGD1A, PET100, PET117, PNKD, SCO1, SCO2, SMIM20, SURF1, TACO1, TIMM21, TMEM177

# Complex V

# CV subunits

ATP5F1A, ATP5F1B, ATP5F1C, ATP5F1D, ATP5F1E, ATP5IF1, ATP5MC1, ATP5MC2, ATP5MC3, ATP5MD, ATP5ME, ATP5MF, ATP5MG, ATP5MPL, ATP5PB, ATP5PD, ATP5PF, ATP5PO, DMAC2L, MT-ATP6, MT-ATP8

# CV assembly factors

ATPAF1, ATPAF2, ATPSCKMT, FMC1, TMEM70

# FAO - Fatty Acid Oxidation

DECR1, HSD17B10, ACAA2, ACAT1, ACACB, ACSS1, ACOT11, AMACR, CRAT, CPT1A, CPT1B, CPT2, ETFA, ETFB, ETFDH, ECI1, ECI2, ECHS1, HADH, ACSL1, ACSF2, ACADM, MCEE, MMUT, SLC25A20, CROT, PCCA, PCCB, ACADS, ACADSB, HADHA, HADHB, ACADVL

# TCA - citric acid cycle

OGDH, ACO2, FAHD1, ACLY, CS, D2HGDH, DLD, DLST, FH, IDH3A, IDH3B, IDH3G, IDH2, L2HGDH, MDH2, SLC25A11, MPC1, MPC2, ME2, ME3, PCK2, PC, ABHD11, SUCLA2, SUCLG1, SUCLG2, SLC25A1

# Results



**Supplementary Fig 2.** Electron micrograph of muscle tissue in one patient (P1). a) Subsarcolemmal accumulation of pleomorphic mitochondria with dens matrix causing an overall dark appearance of the mitochondria. b) Some of the mitochondria show dark, round inclusions (arrows).



**Supplementary Fig 3.** Electron micrograph of muscle tissue in one patient (P2). a) The accumulation of mitochondria with electron-dense matrix causing an overall dark appearance. They are located in the sub-sarcolemmal region (arrow) as well as in the intermyofibrillar compartment associated with lipid storage (arrow heads). b and c) Many of the mitochondria show electron dense, round inclusions of various sizes (arrows).



**Supplementary Fig 4.** Complex I activity (NDUFB8 immunofluorescence, green colour) in single muscle fibers. One control and 11 patients (P1-11). The Complex I immunofluorescence is reduced in all patients. Yellow color corresponds to perlecan, a basement membrane protein.

proteomic a	inalysis				
Gene Symbol	UniProt	Description	Unique	log2	FDR
	Accession		Peptides	FC	
CI subunits			<b>^</b>		
NDUFV3	P56181	NADH dehydrogenase [ubiquinone] flayoprotein 3, mitochondrial	2	-1.88	0.00
NDUEC1	043677	NADH dehydrogenose [ubiquinone] 1 subunit C1 mitochondrial	-2	1.60	0.00
NDUFCI	075290	NADII deliyarogenase [ubiquinone] i subunit e1, initoenonariai	2	-1.09	0.00
NDUF 50	0/5380	NADH denydrogenase [ubiquinone] iron-sulfur protein 6, mitochondrial	/	-1.05	0.00
NDUFA/	095182	NADH dehydrogenase [ubiquinone] I alpha subcomplex subunit /	4	-1.64	0.00
NDUFB4	O95168	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 4	4	-1.63	0.00
NDUFS4	O43181	NADH dehydrogenase [ubiquinone] iron-sulfur protein 4, mitochondrial	3	-1.63	0.00
NDUFA2	O43678	NADH dehvdrogenase [ubiquinone] 1 alpha subcomplex subunit 2	5	-1.62	0.00
MT-ND4	P03905	NADH-ubiquinone oxidoreductase chain 4	1	-1.61	0.00
NDUEA10	005200	NADH dehydrogenese [ubiquinone] 1 alpha subcomplex subunit 10	14	1.61	0.00
NDUIAIU	093299	wite show driel	14	-1.0	0.00
	0.0 (770.0		-	1 50	0.00
NDUFAII	Q86Y39	NADH dehydrogenase [ubiquinone] I alpha subcomplex subunit I I	5	-1.58	0.00
NDUFA9	Q16795	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 9,	16	-1.57	0.00
		mitochondrial			
NDUFB8	O95169	NADH dehvdrogenase [ubiquinone] 1 beta subcomplex subunit 8.	4	-1.56	0.00
		mitochondrial			
NDUE A 12	0011100	NADU dahudraganaga [uhiguinana] 1 alnha guhaamnlay guhunit 12	7	1.56	0.00
NDUFA12	Q90109	NADH denydrogenase [ubiquinone] 1 aipna subcomplex subunit 12	1	-1.50	0.00
NDUFB/	P1/568	NADH dehydrogenase [ubiquinone] I beta subcomplex subunit /	6	-1.56	0.00
NDUFV1	P49821	NADH dehydrogenase [ubiquinone] flavoprotein 1, mitochondrial	15	-1.51	0.00
NDUFS1	P28331	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial	35	-1.5	0.00
NDUFS5	O43920	NADH dehvdrogenase [ubiquinone] iron-sulfur protein 5	7	-1.48	0.00
NDUFR9	09Y6M9	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 9	6	-1 48	0.00
NDUED2	042676	NADII dehydrogenose [ubiquinone] 1 beta subcomplex subunit 2	4	1.40	0.00
NDUFB5	043676	NADH denydrogenase [ubiquinone] 1 beta subcomplex subunit 3	4	-1.42	0.00
NDUFBI	075438	NADH dehydrogenase [ubiquinone] I beta subcomplex subunit I	2	-1.41	0.00
NDUFA13	Q9P0J0	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 13	5	-1.40	0.00
NDUFC2	O95298	NADH dehydrogenase [ubiquinone] 1 subunit C2	5	-1.40	0.00
NDUFB6	095139	NADH dehvdrogenase [ubiquinone] 1 beta subcomplex subunit 6	4	-1.36	0.00
NDUE A 8	P51070	NADH dehydrogenose [ubiquinone] 1 alpha subcomplex subunit 8	6	1 3 2	0.00
NDUED10	00(000	NADII deliyarogenase [ubiquinone] 1 apria subcomplex subunit 8	0	1.02	0.00
NDUFBIO	096000	NADH denydrogenase [ubiquinone] 1 beta subcomplex subunit 10	0	-1.27	0.00
NDUFB5	043674	NADH dehydrogenase [ubiquinone] I beta subcomplex subunit 5,	5	-1.27	0.00
		mitochondrial			
NDUFV2	P19404	NADH dehydrogenase [ubiquinone] flavoprotein 2, mitochondrial	9	-1.26	0.00
NDUFA6	P56556	NADH dehvdrogenase [ubiquinone] 1 alpha subcomplex subunit 6	4	-1.19	0.00
NDUER11	09NX14	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 11	3	_1.10	0.00
NDOIDII	QJINAI	mitashan drial	5	-1.10	0.00
	20005			1.0.1	0.01
MT-ND3	P03897	NADH-ubiquinone oxidoreductase chain 3	1	-1.04	0.01
MT-ND5	P03915	NADH-ubiquinone oxidoreductase chain 5	1	-0.84	0.00
NDUFS2	O75306	NADH dehydrogenase [ubiquinone] iron-sulfur protein 2, mitochondrial	13	-0.82	0.00
NDUFS3	O75489	NADH dehvdrogenase [ubiquinone] iron-sulfur protein 3, mitochondrial	7	-0.82	0.00
NDUES7	075251	NADH dehydrogenase [ubiquinone] iron-sulfur protein 7 mitochondrial	4	-0.79	0.00
NDUE 45	016718	NADH dehydrogenese [ubiquinone] 1 elnha guhaempley guhunit 5	1	0.79	0.00
NDUFAS	Q10/18	NADII denydrogenase [ubiquinone] i aipira subcomplex subunit 5	4	-0.76	0.00
NDUF 58	000217	NADH denydrogenase [ubiquinone] iron-sulfur protein 8, mitochondrial	2	-0.75	0.00
NDUFAB1	O14561	Acyl carrier protein, mitochondrial	2	0.20	0.4
CI assembly fa	ctors				
AIFM1	095831	Apoptosis-inducing factor 1 mitochondrial	21	0.14	0 44
NURPI	O8TB37	Iron-sulfur cluster transfer protein NI IBPI	4	0.14	0.70
TMEM126	001061	Transmembrane materin 1264 OS-Hama coniens	-	0.14	0.70
I MEMIZO	Q9H001	Transmemorane protein 120A OS-nomo sapiens	5	0.50	0.55
A					
NDUFAF7	Q7L592	Protein arginine methyltransferase NDUFAF7, mitochondrial	1	0.51	0.11
NDUFAF5	Q5TEU4	Arginine-hydroxylase NDUFAF5, mitochondrial	2	0.74	0.01
ACAD9	09H845	Complex Lassembly factor ACAD9, mitochondrial	8	0.78	0.01
NDUEAE2	O8N183	NADH dehydrogenase [ubiquinone] 1 alpha subcompley assembly factor 2	8	0.92	0.01
NDUE AE6	02201/105	NADH dehydrogenese (ubiquinone) a ampley L assembly factor 6	2	0.02	0.01
NDUFAF0	Q350K2	NADIT denydrogenase (dolquinone) complex 1, assembly factor o	5	0.92	0.01
IMEM/0	QAROR/	I ransmembrane protein 70, mitochondrial	4	0.97	0.02
NDUFAF1	Q9Y375	Complex I intermediate-associated protein 30, mitochondrial	1	0.97	0.00
COA1	Q9GZY4	Cytochrome c oxidase assembly factor 1 homolog	1	0.99	0.01
NDUFAF3	O9BU61	NADH dehvdrogenase [ubiquinone] 1 alpha subcomplex assembly factor 3	5	1.22	0.00
ECSIT	09B095	Evolutionarily conserved signaling intermediate in Toll nathway	1	1.55	0.00
20011	210215	mitochondrial			0.00
	0000022		0	1.57	0.00
NDUFAF4	Q9P032	NADH denydrogenase [ubiquinone] I alpha subcomplex assembly factor 4	8	1.57	0.00
TIMMDC1	Q9NPL8	Complex I assembly factor TIMMDC1, mitochondrial	2	2.02	0.02
<b>CII</b> subunits					
SDHD	014521	Succinate dehydrogenase [ubiquinone] cytochrome b small subunit	2	-0.69	0.03
50110	017021	mitochondrial	-	0.07	0.05
CDUA	D21040	Innovnondilai	25	0.02	0.01
SDHA	P31040	Succinate denydrogenase [ubiquinone] flavoprotein subunit, mitochondrial	25	-0.62	0.01
SDHB	P21912	Succinate dehydrogenase [ubiquinone] iron-sulfur subunit, mitochondrial	15	-0.61	0.01
SDHC	Q99643	Succinate dehydrogenase cytochrome b560 subunit, mitochondrial	2	-0.58	0.01

# Supplementary Table 4. List of proteins detected in subunits and assembly factors for complex I - V in the proteomic analysis

MT-CVB         P00156         Cytochrome b-1         1         4.00         0.89           UQCREC1         P12805         Cytochrome b-1         complex subunit 7, inticchondrial         22         0.16         0.36           UQCRC1         P12805         Cytochrome b-1         complex subunit 7, inticchondrial         18         0.17         0.33           UQCR0         0.1930         Cytochrome b-1         complex subunit 7, inticchondrial         10         0.46         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.02         0.91           UVRNT         Cytochrome b-1         complex subunit 6, mitochondrial         1         0.02         0.91           UVRNT         Complex H assembly factor 1         8         1.17         0.00         0.02         0.91           UVRC1         Optimization factor 1/VRNT         3         0.02         0.91         0.91         0.91         0.91         0.91         0.91         0.91         0.91         0.91         0.91         0.91         0.91         0.91         0.91         0.91         0.91	<b>CIII</b> subunits					
UQCRN2         P47985         Cytochrome b-1 complex subunit 2, mitochondrial         28         0.16         0.36           UQCRC1         P13930         Cytochrome b-1         complex subunit 2, mitochondrial         18         0.17         0.31           UQCR0         Q0390         Cytochrome b-1         complex subunit 3         16         0.17         0.31           UQCR0         P04995         Cytochrome b-1         complex subunit 7         6         0.019         0.02           UQCR0         P14927         Cytochrome b-1         complex subunit 7         6         0.019         0.02         0.94           UVCR1         P03914         Cytochrome b-1         complex subunit 7         3         0.02         0.94           UVCR2         Q9BR12         Ubiguinol-cytochrome conducta subunit 3         1         0.17         0.01           UVCR2         Q9BR12         Ubiguinol-cytochrome conducta subunit 3         1         0.07         0.01           UVCC1         Q9NVA1         Ubiguinol-cytochrome conducta subunit 3         1         0.07         0.01         0.00           UVCC1         Q9NVA1         Ubiguinol-cytochrome conducta subunit 3         1         0.07         0.01         0.01         0.01         0.01	MT-CYB	P00156	Cytochrome b	1	-0.02	0.89
UQCRC1         P2480         Cynothrome b-1 complex suburit 1, mitochondrial         12         0         0         .59           UQCRC1         P39N         Cynothrome b-1 complex suburit 3         1         0         0.45           UQCRC1         P19N         Cynothrome b-1 complex suburit 7         6         0         0.19         0.23           UQCR1         P0497         Cynothrome b-1 complex suburit 7         6         0.01         0.23           UQCR1         P0497         Cynothrome b-1 complex suburit 7         0         0.02         0.94           UQCR1         P0497         Cynothrome b-1 complex suburit 7         0         0.02         0.94           UQCR1         P0497         Cynothrome b-1 complex suburit 7         0         0.02         0.94           USCR1         Q94726         Mitochrome b-1 complex suburit 7         1         0.02         0.94           USCR1         Q94726         Mitochrome b-1 complex suburit 7         1         0.01         0.02         0.94           USCR1         Q94726         Mitochromit 16         1         0.75         0.11         0.00           USCC1         Q94736         Mitochrome condiase suburit 7         1         0.02         0.02         0.02	UQCRFS1	P47985	Cytochrome b-c1 complex subunit Rieske, mitochondrial	8	0.13	0.45
OUCREAT         Cybertome betty atomine type is submit 1, minechondrial         18         0         0.17         0.33           UGCRB         O14949         Cybertome betty and type is submit 7         6         0.19         0.23           UGCRB         P14927         Cybertome betty and type is submit 7         6         0.19         0.23           UCCRH         P07919         Cybertome betty and type is submit 7         6         0.00         0.44           UVCCR         P07917         Cybertome betty and type is submit 7         3         0.02         0.94           UVCCR         P07926         Mitchone and type is submit 7         3         0.02         0.94           UVCCR         P08147         Cybertome betty and type is submit 74         1         1         1         0.00           UVCC2         Q918417         Ubiputo-cybertome cybertome cybertome type is submit 74         1         1         0.01         0.01           COX7A         P23410         Cybertome cybertome cybertome type is submit 74         1         1         0.02         0.03         0.01           COX7A         P23410         Cybertome c	UQCRC2	P22695	Cytochrome b-c1 complex subunit 2, mitochondrial	22	0.16	0,.36
UCK00         O. 14949         Cynchrome b-1 complex submit 3         4         0.11         0.33           UCK11         P0875         Cynchrome b-1 complex submit 7         6         0.19         0.23           UCK11         P0719         Cynchrome b-1 complex submit 6, mitochondrial         10         0.46         0.00           CH1         assembly factor         1         0.00         0.94         0.00           UCC21         P0719         Cynchrome b-1 complex submit 7, mitochondrial         4         0.14         0.00           UCC31         P0717         Mitochondrial dhaperone BCS1         4         1.17         0.00           UCC41         P0714         Cynchrome coxidas submit 7, mitochondrial         1         0.75         0.11           COX7A1         P24311         Cynchrome coxidas submit 7, mitochondrial         1         0.75         0.11           COX7A1         P24311         Cynchrome coxidas submit 7, mitochondrial         2         0.63         0.01           COX7A1         P24311         Cynchrome coxidas submit 7, Mitochondrial         7         4.51         0.02           COX7A1         P24311         Cynchrome coxidas submit 7, Mitochondrial         7         4.51         0.02           COX7A2 <td>UQCRUI</td> <td>P31930</td> <td>Cytochrome b-c1 complex subunit 1, mitochondrial</td> <td>18</td> <td>0.17</td> <td>0.29</td>	UQCRUI	P31930	Cytochrome b-c1 complex subunit 1, mitochondrial	18	0.17	0.29
UQCRB         P1492         Cycochrome c b-el complex subunit 7         6         0.19         0.28           CYCI         P08574         Cytochrome c b-el complex subunit 6, mitochondrial         4         0.89         0.00           ULRAT         QUSX0         Complex III assembly factor LYRM7         3         0.02         0.94           UCC2         Q9BRT2         Ubiquinol-cytochrome c reductsa complex assembly factor 2         2         0.95         0.00           CVC2         Q9RN7A         Ubiquinol-cytochrome c reductsa complex assembly factor 1         8         1.17         0.00           CVC2         Q9NYA1         Ubiquinol-cytochrome c reductsa complex assembly factor 1         8         1.17         0.00           CVX subunit         QV276         Mitochandrial dagrocone RCS1         4         1.4         0.00           COXC1         QPN7A         Ubicherome c oxidas subunit 7.         mitochondrial         2         -0.71         0.01           COXT3         P2410         Cytochrome c oxidas subunit 6.         4         -0.62         0.03           COXT4         P2410         Cytochrome c oxidas subunit 6.         4         -0.62         0.03           COXT6         P99660         Cytochrome c oxidas subunit 6.         4         -0.	UQCRIO	014949	Cytochrome b-c1 complex subunit 8	4	0.17	0.40
	UOCRB	P14927	Cytochrome b-c1 complex subunit 7	6	0.19	0.28
UQCRH         P07919         Cytochrome b=1 complex subunit 6, mitochondrial         4         0.89         0.00           CHI assembly factors           0.02         0.94           UVCC2         Q9BRT2         Ubigatinol-cytochrome c reductase complex assembly factor 2         2         0.93         0.00           UCC2         Q9NYA1         Ubigatinol-cytochrome c reductase complex assembly factor 1         8         1.11         0.00           UCC21         Q9NYA1         Ubigatinol-cytochrome c reductase complex assembly factor 1         8         1.17         0.00           CV subunits         Cytochrome c oxidase subuni 7, mitochondrial         2         -0.71         0.01           COX7A1         P24101         Cytochrome c oxidase subuni 7, mitochondrial         1         -0.70         0.01           COX7A5         P24310         Cytochrome c oxidase subuni 6C         4         -0.62         0.01           COX7A6         P24354         Cytochrome c oxidase subuni 7A         -0.51         0.02         0.02         0.02         0.02         0.03         0.044         0.03         0.044         0.03         0.044         0.03         0.044         0.03         0.044         0.03         0.044         0.03         0.03         0.03 <td>CYC1</td> <td>P08574</td> <td>Cytochrome c1, heme protein, mitochondrial</td> <td>10</td> <td>0.46</td> <td>0.03</td>	CYC1	P08574	Cytochrome c1, heme protein, mitochondrial	10	0.46	0.03
CIII assembly factor         9           LYRM7         QSUSM0         Complex III assembly factor LYRM7         3         0.02         0.94           UQCC2         QPV7A         Umquinol-cytochrome f8CS1         4         1.117         0.00           UGC31         QPV7A         Umquinol-cytochrome f8CS1         4         1.117         0.00           CV submits         MT-CO3         P0014         Cytochrome c oxidase submit 3         1         -0.75         0.11           COXTA1         P24110         Cytochrome c oxidase submit 7A, inticchondrial         2         -0.70         0.01           COXTC         P1954         Cytochrome c oxidase submit 6B         -0.75         0.02         0.02           COXAGE         P0966         Cytochrome c oxidase submit 6B         -0.62         0.03         0.02         0.02         0.01         COXAGE         P0960         Cytochrome c oxidase submit 2         -0.51         0.02         0.01         COXAB         P1454         Cytochrome c oxidase submit 3         intochondrial         1         -0.44         0.02         COXAB         P1446         Cytochrome c oxidase submit 7A callead protein, mitochondrial         1         0.03         0.01         COXAB         P1446         Cytochrome c oxidase submit 7A callead protein, monlog	UQCRH	P07919	Cytochrome b-c1 complex subunit 6, mitochondrial	4	0.89	0.00
UKBM7         G91/S00         Complex III assembly factor 1/RM7         3         0.02         0.44           UQCC2         Q98172         Ubiquinol-systemburg reductase complex assembly factor 1         4         1.14         0.00           UQCC1         Q98172         Ubiquinol-systemburg reductase complex assembly factor 1         8         1.17         0.00           UCC21         Q9NVAI         Ubiquinol-systemburg reductase complex assembly factor 1         8         1.17         0.00           COX abunits         The Co3         P00414         Cytochrome c oxidase subuni 7.8, mitochondrial         2         -0.71         0.01           COX7A         P24310         Cytochrome c oxidase subuni 7.8, mitochondrial         2         -0.63         0.01           COX7B         P24311         Cytochrome c oxidase subuni 6.2         -0.63         0.02         0.02         0.02         0.02         0.03         0.02         0.03         0.02         0.02         0.03         0.04         0.02         0.03         0.04         0.02         0.03         0.04         0.02         0.03         0.04         0.02         0.03         0.04         0.02         0.03         0.04         0.02         0.04         0.02         0.03         0.03         0.03	CIII assembly	factors				
UQCC2         OPHRT2         Ubiquinol-sytochromic e reductase complex assembly factor 1         2         0.95         0.00           UCC1         OPY276         Miccohondrial chaperene BCS1         4         1.14         0.00           CIV subunits         MT-C03         P00414         Cytochrome c oxidase subunit 7A1, mitochondrial         2         -0.71         0.01           COX7A1         P24310         Cytochrome c oxidase subunit 7A1, mitochondrial         2         -0.63         0.01           COX7C         P19394         Cytochrome c oxidase subunit 7C, mitochondrial         2         -0.63         0.01           COX7C         P19394         Cytochrome c oxidase subunit 7C, mitochondrial         7         -0.51         0.02           COX7B         P04605         Cytochrome c oxidase subunit 7C, mitochondrial         7         -0.51         0.02           DUTA4         OpH8945         Cytochrome c oxidase subunit 7A         5         0.40         0.03           COX7A         P14946         Cytochrome c oxidase subunit 7A         1         -0.41         0.02           COX7A         P1406         Cytochrome c oxidase subunit 7A-related protein, mitochondrial         2         0.19         0.51           COX7A2         D14546         Cytochrome c oxidase subu	LYRM7	O5U5X0	Complex III assembly factor LYRM7	3	0.02	0.94
BCS1L         Q9Y276         Micechandrai chaperone BCS1         4         1.14         0.00           CIV subunits         mtrc03         P00414         Cynchrome c oxidase subunit 3         1         0.00           COX7A1         P24310         Cynchrome c oxidase subunit 71, mitochondrial         2         0.67         0.01           COX7A         P24311         Cynchrome c oxidase subunit 71, mitochondrial         2         0.63         0.01           COX7A         P24311         Cynchrome c oxidase subunit 71, mitochondrial         2         0.63         0.01           COX7AB         P24310         Cynchrome c oxidase subunit 61         6         0.52         0.02           COX5B         P10606         Cynchrome c oxidase subunit 151, mitochondrial         7         0.51         0.02           NUFLA4         C00493         Cynchrome c oxidase subunit 3A, mitochondrial         7         0.51         0.02           NUFLA4         C00493         Cynchrome c oxidase subunit 3A, mitochondrial         7         0.51         0.02           COX5A         P20674         Cynchrome c oxidase subunit 3A, mitochondrial         2         0.01         0.99           COX7AL         P1496         Cynchrome c oxidase subunit 3A, mitochondrial         2         0.01	UQCC2	Q9BRT2	Ubiquinol-cytochrome c reductase complex assembly factor 2	2	0.95	0.00
UQCCI         Q9NVA1         Ubiquinol-cytochrome c reductase complex assembly factor 1         8         1.17         0.00           CIV subunits         MT-C03         P00414         Cytochrome c oxidase subunit 7A1, mitochondrial         1         -0.75         0.11           COX7A1         P24311         Cytochrome c oxidase subunit 7A1, mitochondrial         2         -0.75         0.11           COX7C         P15954         Cytochrome c oxidase subunit 7C, mitochondrial         2         -0.63         0.01           COX7C         P15954         Cytochrome c oxidase subunit 7C, mitochondrial         7         -0.51         0.02           COX6B         P14854         Cytochrome c oxidase subunit 7B, mitochondrial         7         -0.51         0.02           MUC7A         000483         Cytochrome c oxidase subunit 7A, mitochondrial         7         -0.37         0.83           COX7A1         P14406         Cytochrome c oxidase subunit 7A, mitochondrial         2         0.01         0.99           COX7A2         P14406         Cytochrome c oxidase subunit 7A, mitochondrial         2         0.02         0.94           COX1A2         P14406         Cytochrome c oxidase subunit 7A, related protein indochondrial         2         0.01         0.91           COX1A2         <	BCS1L	Q9Y276	Mitochondrial chaperone BCS1	4	1.14	0.00
CIV subunits         Visit subunit 7A1, mitochondrial         1         -0.75         0.11           COX7A         P4311         Cytochrome c oxidase subunit 7A1, mitochondrial         1         -0.07         0.01           COX7A         P4311         Cytochrome c oxidase subunit 7A1, mitochondrial         1         -0.05         0.011           COX7A         P4411         Cytochrome c oxidase subunit 9B         CoX7A         0.021         -0.05         0.002           COX7A         P10066         Cytochrome c oxidase subunit 7D         -0.05         -0.05         0.011         -0.05         -0.05         0.010         COX7A         P1006         Cytochrome c oxidase subunit 7A2, mitochondrial         -0.02         0.944         0.021         0.044         0.030         0.010         0.021         COX7A2         CP1066         Cytochrome c oxidase subunit 7A2, mitochondrial         2         0.021         0.020	UQCC1	Q9NVA1	Ubiquinol-cytochrome c reductase complex assembly factor 1	8	1.17	0.00
MT-C03         P00414         Cytochrome c oxidase suburit 31         1         0-075         0.11           COX7A         P24310         Cytochrome c oxidase suburit 71, mitochondrial         2         0-071         0.01           COX7B         P24311         Cytochrome c oxidase suburit 76, mitochondrial         2         0-063         0.01           COX7C         P19594         Cytochrome c oxidase suburit 76         4         0-652         0.01           COX6B         P10606         Cytochrome c oxidase suburit 76         7         -0.51         0.02           NUTCA2         P00403         Cytochrome c oxidase suburit 74         7         -0.51         0.02           NUTCA4         P00403         Cytochrome c oxidase suburit 74         7         -0.51         0.02           NUTCA4         P00403         Cytochrome c oxidase suburit 74, mitochondrial         2         0.10         0.99           COX5A         P20674         Cytochrome c oxidase suburit 7A, mitochondrial         2         0.10         0.99           COX6A         P20674         Cytochrome c oxidase assembly factor 6 homolog         1         0.03         0.91           COX6         SytTa         Cytochrome c oxidase assembly factor 6 homolog         2         0.01         0.94 <td>CIV subunits</td> <td></td> <td></td> <td></td> <td></td> <td></td>	CIV subunits					
COX7A1         P24311         Cytochrome c oxidase submit 7A1, mitochondrial         1         -0.71         0.01           COX7C         P19594         Cytochrome c oxidase submit 7C, mitochondrial         2         -0.63         0.01           COX7C         P19594         Cytochrome c oxidase submit 6B         4         -0.62         0.01           COX6B1         P14854         Cytochrome c oxidase submit 7B         7         -0.51         0.02           COX5B         P16666         Cytochrome c oxidase submit 7B         7         -0.51         0.02           MUCA20         P00403         Cytochrome c oxidase submit 7A         7         -0.51         0.02           COXA11         P13073         Cytochrome c oxidase submit 7A         mitochondrial         7         -0.51         0.02           COXA1         P14066         Cytochrome c oxidase submit 7A.mitochondrial         7         -0.03         0.91           COX7A2         P14066         Cytochrome c oxidase submit 7A.mitochondrial         2         0.01         0.99           COX7A2         P14066         Cytochrome c oxidase assembly factor 3 homolog.         2         0.03         0.91           CM1         OZ7K0         COX         Sasenbly ininichondrial protein COX11,mitochondrial <t< td=""><td>MT-CO3</td><td>P00414</td><td>Cytochrome c oxidase subunit 3</td><td>1</td><td>-0.75</td><td>0.11</td></t<>	MT-CO3	P00414	Cytochrome c oxidase subunit 3	1	-0.75	0.11
COX7B         P24311         Cytochrome c oxidase subunit 7E, mitochondrial         2         -0.63         0.01           COX7C         P19594         Cytochrome c oxidase subunit 6C         4         -0.63         0.01           COX6B         P10606         Cytochrome c oxidase subunit 5B, mitochondrial         6         -0.62         0.03           COX5B         P10606         Cytochrome c oxidase subunit 5B, mitochondrial         7         -0.51         0.02           NUTCA2         P00403         Cytochrome c oxidase subunit 7A, mitochondrial         7         -0.44         0.03           COX5A         P21674         Cytochrome c oxidase subunit 7A, related protein, mitochondrial         7         -0.37         0.08           COX7A2         D14548         Cytochrome c oxidase subunit 7A, related protein, mitochondrial         2         0.01         0.99           COX6         921406         Cytochrome c oxidase subunit 7A, related protein, mitochondrial         2         0.03         0.91           COX6         921406         Cytochrome c oxidase assembly factor 6 homolog         2         0.03         0.91           COX6         92720R         Cytochrome c oxidase assembly refore for SD homolog, mitochondrial         2         0.01         0.49         0.03         0.14         0.04 <td>COX7A1</td> <td>P24310</td> <td>Cytochrome c oxidase subunit 7A1, mitochondrial</td> <td>2</td> <td>-0.71</td> <td>0.01</td>	COX7A1	P24310	Cytochrome c oxidase subunit 7A1, mitochondrial	2	-0.71	0.01
COX7C         P15954         Cytochrome c oxidase subunit 7C, mitochondrial         2         0.66         0.01           COX8C         P09669         Cytochrome c oxidase subunit 6B1         6         0.62         0.03           COX5B         P14854         Cytochrome c oxidase subunit 3B, mitochondrial         7         -0.51         0.02           MT-CO2         P00403         Cytochrome c oxidase subunit 3B, mitochondrial         7         -0.51         0.02           COXAI1         P13073         Cytochrome c oxidase subunit 3A, mitochondrial         7         -0.51         0.02           COXA1         P10606         Cytochrome c oxidase subunit 7A, mitochondrial         7         -0.44         0.03           COX7A2         P14406         Cytochrome c oxidase subunit 7A, mitochondrial         2         0.01         0.99           COX7A2         P14406         Cytochrome c oxidase assembly factor 6 homolog         1         0.03         0.91           COA6         O3713         Cytochrome c oxidase assembly factor 6 homolog, mitochondrial         2         0.010         0.90           COA6         O3713         Cytochrome c oxidase assembly factor 6 homolog, mitochondrial         3         0.38         0.00           COX10         O940807         Cytochrome c oxidase ass	COX7B	P24311	Cytochrome c oxidase subunit 7B, mitochondrial	1	-0.70	0.01
COX6C         P09609         Cytochrome c oxidase subunit 6B1         6         -0.62         0.03           COX5B         P10606         Cytochrome c oxidase subunit 78, mitochondrial         7         -0.51         0.02           MT-CO2         P00403         Cytochrome c oxidase subunit 76         7         -0.51         0.02           NUFA4         O00483         Cytochrome c oxidase subunit 76         7         -0.51         0.02           COX5A         P20674         Cytochrome c oxidase subunit 7A-related protein, mitochondrial         7         -0.37         0.08           COX5A         P20674         Cytochrome c oxidase subunit 7A-related protein, mitochondrial         2         0.019         0.51           CV assembly factors         PET100         POD107         Protein PET100 homolog, mitochondrial         2         0.02         0.94           CMC1         Q727K0         COX assembly mitochondrial protein COX19         1         0.38         0.01           COA6         Q51713         Cytochrome c oxidase assembly protein COX19         3         0.38         0.01           COX10         Q91780         Cytochrome c oxidase assembly protein COX19         3         0.38         0.01           COX11         Q91805         Cytochrome c oxidase assembly protei	COX7C	P15954	Cytochrome c oxidase subunit 7C, mitochondrial	2	-0.63	0.01
COX5B         P10606         Cytochrome c oxidase subunit SB, mitochondrial         7         -0.51         0.02           MT-CO2         P00403         Cytochrome c oxidase subunit SB, mitochondrial         7         -0.51         0.02           MT-CO2         P00403         Cytochrome c oxidase subunit NDUFA4         5         -0.44         0.02           COXAII         P1377         Cytochrome c oxidase subunit A, mitochondrial         7         -0.51         0.02           COXA2         P14406         Cytochrome c oxidase subunit 7A, mitochondrial         2         0.01         0.99           COX7A2         P14406         Cytochrome c oxidase subunit 7A, mitochondrial         2         0.01         0.99           COX7A2         P14406         Cytochrome c oxidase subunit 7A, related protein, mitochondrial         2         0.02         0.94           COA6         Q3T35         Cytochrome c oxidase assembly factor 6 homolog         1         0.03         0.91           COX11         Q9T27K0         COX assembly mitochondrial protein 2 homolog         1         0.38         0.14           COX11         Q9H96         Cytochrome c oxidase assembly protein COX14         0.38         0.01           TMC11         Q9F36         Cytochrome c oxidase assembly protein COX14 <td< td=""><td>COX6C</td><td>P09669</td><td>Cytochrome c oxidase subunit 6C</td><td>4</td><td>-0.62</td><td>0.01</td></td<>	COX6C	P09669	Cytochrome c oxidase subunit 6C	4	-0.62	0.01
COX5B         P10000         Cytochrome c oxidase subunit 3B, mitochondrial         7         -0.51         0.02           NULFA4         000483         Cytochrome c oxidase subunit 3form 1, mitochondrial         11         -0.44         0.02           COX411         P13073         Cytochrome c oxidase subunit 3form 1, mitochondrial         1         -0.44         0.02           COX5A         P20674         Cytochrome c oxidase subunit 7A, mitochondrial         2         0.010         0.99           COX7A2L         O14548         Cytochrome c oxidase subunit 7A, related protein, mitochondrial         2         0.02         0.94           CMC         OXA2L         O14548         Cytochrome c oxidase assembly factors         9         9         0.51           CV assembly mitochondrial protein homolog         1         0.03         0.91         0.03         0.91           COA6         Q9XR0         Cytochrome c oxidase assembly factors homolog         1         0.38         0.14           COX19         Q9MR0         Cytochrome c oxidase assembly protein COX11         3         0.38         0.00           TMM21         Q9KN1         Cytochrome c oxidase assembly protein COX14         1         0.74         0.62         0.01           TACC1         Q9BNH <td< td=""><td>COX6B1</td><td>P14854</td><td>Cytochrome c oxidase subunit 6B1</td><td>6</td><td>-0.52</td><td>0.03</td></td<>	COX6B1	P14854	Cytochrome c oxidase subunit 6B1	6	-0.52	0.03
M1-CO2         P00-00         Cynchrome c oxidase subunit NDUFA4         7         -0.31         0.02           COXAII         P1307         Cynchrome c oxidase subunit A, mitochondrial         11         -0.44         0.02           COXAII         P1406         Cynchrome c oxidase subunit A, mitochondrial         7         -0.37         0.08           COX7A2         P14406         Cynchrome c oxidase subunit 7A, mitochondrial         2         0.01         0.99           COX7A2         P14406         Cynchrome c oxidase subunit 7A, mitochondrial         2         -0.02         0.94           CVF assembly factors          PetT100         P0D107         Protein PET100 homolog, mitochondrial         2         -0.02         0.94           COA         Q9T2R0         Cynchrome c oxidase assembly factor 6 homolog         1         0.03         0.91           COA         Q9T2R0         Cynchrome c oxidase assembly protein COX1         1         0.38         0.14           COX1         Q9T2R0         Cynchrome c oxidase assembly protein COX1         3         0.38         0.01           TACOI         Q9T8R0         Cynchrome c oxidase assembly protein COX1         3         0.38         0.01           COX11         Q9T8N0         Cynchrome c oxidase assembl	COX5B	P10606	Cytochrome c oxidase subunit 5B, mitochondrial	7	-0.51	0.02
NDD17A+         Coversionel Covidase subunit NDD17A+         5         -0-47         0.02           COX411         P13073         Cytochrome coxidase subunit 3A, mitochondrial         7         -0.37         0.08           COX5A         P20674         Cytochrome coxidase subunit 7A, mitochondrial         2         0.01         0.99           COX7A2L         O14548         Cytochrome coxidase subunit 7A, chitochondrial         2         0.01         0.99           COX7A2L         O14548         Cytochrome coxidase subunit 7A, chitochondrial         2         -0.02         0.94           CMC1         Q7CzNK0         COX assembly mitochondrial protein homolog         1         0.03         0.91           COA6         Q51713         Cytochrome coxidase assembly factor 3 homolog, mitochondrial         4         0.29         0.18           COX10         Q7tochrome coxidase assembly protein COX11         0.04         0.38         0.14           COX11         Q94P80         Cytochrome coxidase assembly protein COX11, mitochondrial         3         0.38         0.00           COX11         Q94P86         Cytochrome coxidase assembly protein COX14         1         0.74         0.02           COX11         Q94P86         Cytochrome coxidase assembly protein COX14         1         0.	MT-CO2	P00403	Cytochrome c oxidase subunit 2	5	-0.51	0.02
COX5A         P1007         Cytochrome c oxidase subunit 3A, mitochondrial         7         -0.37         0.08           COX7A2         P14406         Cytochrome c oxidase subunit 7A, mitochondrial         2         0.01         0.99           COX7A2         P14406         Cytochrome c oxidase subunit 7A, mitochondrial         2         0.19         0.51           CIV assembly factors         PET100         P00J07         Protein PET100 homolog, mitochondrial protein homolog         1         0.03         0.91           COA6         Q51713         Cytochrome c oxidase assembly factor 6 homolog         1         0.03         0.91           COA6         Q51713         Cytochrome c oxidase assembly protein 2 homolog         1         0.38         0.14           COX19         Q49896         Cytochrome c oxidase assembly protein COX19         3         0.38         0.01           TMC11         Q97601         Cytochrome c oxidase assembly protein COX11         1         0.74         0.02         0.01           TACO1         Q98164         Translational assembly protein COX11         1         0.74         0.02         0.01           COX19         Q49896         Cytochrome c oxidase assembly protein COX14         1         0.74         0.02         0.01         COX4	NDUFA4 COX411	P13073	Cytochrome c oxidase subunit A isoform 1 mitochondrial	11	-0.44	0.02
COX7A2         P14406         Cytochrome c oxidase subunit 7A2, mitochondrial         2         0.01         0.99           CIV assembly factors         PET100         PD0107         Protein PET100 homolog, mitochondrial         2         -0.02         0.94           CMC1         Q7Z7K0         COX assembly mitochondrial protein homolog         1         0.03         0.91           COA6         Q7TX0         COX assembly mitochondrial protein homolog         2         0.10         0.49           COA3         Q9Y2R0         Cytochrome c oxidase assembly factor 3 homolog         1         0.38         0.04           COX19         Q9BV67         Cytochrome c oxidase assembly protein COX19         3         0.38         0.00           COX11         Q9F0V1         Vitochrome c oxidase assembly protein COX19         3         0.58         0.01           TMM21         Q9BV7         Mitochondrial mpori inner membrane translocase subuni Tim21         5         0.62         0.01           TAC01         Q9BS14         Translational activator of cytochrome c oxidase assembly protein COX14         1         0.74         0.02           COA7         Q96BB5         Cytochrome c oxidase assembly protein COX14         1         0.74         0.03           COX20         Q58115 <td< td=""><td>COX5A</td><td>P20674</td><td>Cytochrome c oxidase subunit 5A, mitochondrial</td><td>7</td><td>-0.37</td><td>0.03</td></td<>	COX5A	P20674	Cytochrome c oxidase subunit 5A, mitochondrial	7	-0.37	0.03
COX7A2L         O14548         Cytochrome c oxidase subunit 7A-related protein, mitochondrial         2         0.19         0.51           CIV assembly factors         PET100         P0D107         Protein PET100 homolog, mitochondrial         2         -0.02         0.94           CMC1         Q727K0         CX0 cox assembly mitochondrial protein homolog,         1         0.03         0.91           COA6         Q51713         Cytochrome c oxidase assembly factor 6 homolog,         1         0.38         0.04           COX12         Q99RP2         Cox assembly mitochondrial protein 2 homolog,         1         0.38         0.00           COX11         Q9469B6         Cytochrome c oxidase assembly protein COX19         3         0.38         0.00           COX11         Q99F0N1         Cytochrome c oxidase assembly protein COX14         1         0.74         0.62         0.01           TACO1         Q98BH4         Translational activator of cytochrome c oxidase 1         4         6.68         0.01           CX014         Q96136         Cytochrome c oxidase assembly protein COX14         1         0.74         0.02           COX14         Q96136         Cytochrome c oxidase assembly protein COX14         2         0.87         0.01           SCO1         OT5586 </td <td>COX7A2</td> <td>P14406</td> <td>Cytochrome c oxidase subunit 7A2, mitochondrial</td> <td>2</td> <td>0.01</td> <td>0.99</td>	COX7A2	P14406	Cytochrome c oxidase subunit 7A2, mitochondrial	2	0.01	0.99
CIV assembly factors           PET100         PODI07         Protein PET100 homolog, mitochondrial protein homolog         1         0.03         0.91           COA6         Q5TT3         Cytochrome c oxidase assembly factor 6 homolog         2         0.10         0.49           COA3         Q9Y2R0         Cytochrome c oxidase assembly factor 3 homolog, mitochondrial         4         0.29         0.18           CMC2         Q9NRP2         Coxt assembly mitochondrial protein 2 homolog         1         0.38         0.01           COX19         Q49B96         Cytochrome c oxidase assembly protein COX19         3         0.38         0.00           COX11         Q9BVV7         Mitochondrial import inner membrane translocase subunit Tim21         5         0.62         0.01           TACO1         Q9BS1H         Translational activator of cytochrome c oxidase astembly protein COX14         1         0.74         0.02           COA7         Q96BR5         Cytochrome c oxidase assembly protein COX14         1         0.48         0.03           SCO1         O75880         Protein SCO1 homolog, mitochondrial         2         0.87         0.01           COX15         Q7BC1K         Storfeit Deus protein COX15         2         1.44         0.01           DMAC2	COX7A2L	O14548	Cytochrome c oxidase subunit 7A-related protein, mitochondrial	2	0.19	0.51
CV ascinnoy factors         2         -0.02         0.94           CMC1         Q7Z7K0         COX assembly mitochondrial protein homolog         1         0.03         0.91           COA6         QSTT3         Cytochrome c oxidase assembly factor 6 homolog         1         0.03         0.91           COA3         Q9Y2R0         Cytochrome c oxidase assembly factor 6 homolog         1         0.38         0.14           COX19         Q49B96         Cytochrome c oxidase assembly protein COX19         3         0.38         0.00           COX11         Q9BVY0         Cytochrome c oxidase assembly protein COX19         3         0.58         0.01           TIMM21         Q9BVY1         Witochondrial import immermeshocase subunit Tim21         5         0.62         0.01           TACO1         Q9BSH4         Translational activator of cytochrome c oxidase assembly protein COX14         1         0.74         0.02           COA7         Q96BR5         Cytochrome c oxidase assembly protein COX14         1         0.84         0.03           SCO1         O75880         Protein SCO1 homolog, mitochondrial         2         0.87         0.01           SURF1         Q15526         Surfeit locus protein 1         3         0.55         0.00 <t< td=""><td>CIV assambly</td><td>factors</td><td></td><td></td><td></td><td></td></t<>	CIV assambly	factors				
CMC1         Q727K0         COX assembly mitochondrial protein homolog         1         0.03         0.91           COA6         Q3713         Cytochrome c oxidase assembly factor 6 homolog         2         0.10         0.49           COA3         Q9Y2R0         Cytochrome c oxidase assembly factor 6 homolog         1         0.38         0.14           CMC2         Q9NRP2         COX assembly mitochondrial protein COX19         3         0.38         0.00           COX11         Q9H041         Cytochrome c oxidase assembly protein COX11, mitochondrial         3         0.58         0.01           TMM21         Q9BSH4         Translational activator of cytochrome c oxidase 1         4         0.66         0.01           COX14         Q96136         Cytochrome c oxidase assembly protein COX14         1         0.74         0.02           COA7         Q96BS5         Cytochrome c oxidase assembly factor 7         4         0.84         0.03           SCO1         O7880         Frotein SCO2 homolog, mitochondrial         2         0.87         0.01           SCO2         O43819         Protein SCO2 homolog, mitochondrial         2         1.44         0.01           CWX20         QSR115         Cytochrome c oxidase assembly protein COX20, mitochondrial         2	PET100	PODI07	Protein PET100 homolog, mitochondrial	2	-0.02	0.94
COA6         QSJTJ3         Cytochrome c oxidase assembly factor 6 homolog         2         0.10         0.49           COA3         Q9Y2R0         Cytochrome c oxidase assembly factor 3 homolog, mitochondrial         4         0.29         0.18           CMC2         Q9NRP2         COX assembly protein COX19         3         0.38         0.01           COX11         Q9BBH4         Cytochrome c oxidase assembly protein COX19         3         0.38         0.01           TIMM21         Q9BVY7         Mitochondrial import inner membrane translocase subunit Tim21         5         0.62         0.01           TACO1         Q9BSH4         Translational activator of cytochrome c oxidase assembly protein COX14         1         0.74         0.02           COA7         Q96BR5         Cytochrome c oxidase assembly protein COX14         1         0.74         0.02           SCO1         O75880         Protein SCO1 homolog, mitochondrial         2         0.87         0.01           SCO2         O43819         Protein SCO2 homolog, mitochondrial         2         1.14         0.01           COX15         Q7KZN9         Cytochrome c oxidase assembly protein COX15 homolog         2         1.34         0.01           SUF1         Q15526         Surfeit locus protein 1	CMC1	07Z7K0	COX assembly mitochondrial protein homolog	1	0.02	0.91
$\begin{array}{cccc} COA3 & Q9Y2R0 & Cytochrome c oxidase assembly fractor 3 homolog, mitochondrial \\ CMC2 & Q9NRP2 & COX assembly mitochondrial protein COX19 & 1 & 0.38 & 0.14 \\ COX19 & Q49B6 & Cytochrome c oxidase assembly protein COX11 , mitochondrial & 3 & 0.58 & 0.01 \\ COX11 & Q9F6N1 & Cytochrome c oxidase assembly protein COX11, mitochondrial & 3 & 0.58 & 0.01 \\ TMC01 & Q9BSFH4 & Translational activator of cytochrome c oxidase as ubunit Tim21 & 5 & 0.62 & 0.01 \\ TACO1 & Q9BSFH4 & Translational activator of cytochrome c oxidase as ubunit Tim21 & 4 & 0.68 & 0.01 \\ COX14 & Q96136 & Cytochrome c oxidase assembly protein COX14 & 1 & 0.74 & 0.02 \\ COA7 & Q96BR5 & Cytochrome c oxidase assembly factor 7 & 4 & 0.81 & 0.00 \\ SMIM20 & Q8N5C0 & Small integral membrane protein 20 & 1 & 0.84 & 0.03 \\ SCO1 & O75880 & Protein SCO1 homolog, mitochondrial & 2 & 0.87 & 0.01 \\ SCO2 & O43819 & Protein SCO2 homolog, mitochondrial & 3 & 0.98 & 0.01 \\ COX20 & Q5R115 & Cytochrome c oxidase assembly protein COX20, mitochondrial & 2 & 1.14 & 0.01 \\ SUFF1 & Q15526 & Surfeit locus protein 1 & 3 & 1.55 & 0.00 \\ \hline CV submits & & & & & & & & & & & & & & & & & & &$	COA6	Q5JTJ3	Cytochrome c oxidase assembly factor 6 homolog	2	0.10	0.49
CMC2         Q9NRP2         COX assembly mitochondrial protein COX19         1         0.38         0.14           COX19         Q49B96         Cytochrome c oxidase assembly protein COX11, mitochondrial         3         0.38         0.00           COX11         Q9F0N1         Cytochrome c oxidase assembly protein COX11, mitochondrial         3         0.58         0.01           TIMM21         Q9BVY7         Mitochondrial import inner membrane translocase subunit Tim21         5         0.62         0.01           TACO1         Q9BSH4         Translational activator of cytochrome c oxidase assembly fortor         1         0.74         0.02           COA7         Q96BR5         Cytochrome c oxidase assembly fractor 7         4         0.81         0.00           SC01         O75880         Protein SC01 homolog, mitochondrial         2         0.87         0.01           SC02         Q481P         Protein SC02 homolog, mitochondrial         2         1.14         0.01           COX15         Q7KZN9         Cytochrome c oxidase assembly protein COX20, mitochondrial         2         1.34         0.01           COX15         Q7KZN9         Cytochrome c oxidase assembly protein COX20, mitochondrial         2         0.62         0.01           ATP5MG         O75964         ATP	COA3	Q9Y2R0	Cytochrome c oxidase assembly factor 3 homolog, mitochondrial	4	0.29	0.18
COX19         Q49B96         Cytochrome c oxidase assembly protein COX11, mitochondrial         3         0.38         0.00           COX11         Q9BVV7         Mitochondrial import inner membrane translocase subunit Tim21         5         0.62         0.01           TACO1         Q9BSH4         Translational activator of cytochrome c oxidase 1         4         0.68         0.01           COX14         Q96BR5         Cytochrome c oxidase assembly protein COX14         1         0.74         0.02           COA7         Q96BR5         Cytochrome c oxidase assembly protein COX14         1         0.74         0.03           SCO1         O758B0         Protein SCO1 homolog, mitochondrial         2         0.87         0.01           SCO2         Q43R19         Protein SCO2 homolog, mitochondrial         2         1.14         0.01           COX10         Q7SR2N         Cytochrome c oxidase assembly protein COX15 homolog         2         1.34         0.01           SURF1         Q15526         Surfeit locus protein 1         3         1.55         0.00           CV subunits         DMAC2L         Q9766         ATP synthase subunit s, mitochondrial         7         0.49         0.03           TPSF1D         P30049         ATP synthase subunit dita, mitochondrial <td>CMC2</td> <td>Q9NRP2</td> <td>COX assembly mitochondrial protein 2 homolog</td> <td>1</td> <td>0.38</td> <td>0.14</td>	CMC2	Q9NRP2	COX assembly mitochondrial protein 2 homolog	1	0.38	0.14
COX11         Q9Y6N1         Cytochrome c oxidase assembly protein COX11, mitochondrial         3         0.58         0.01           TIMM21         Q9BSH4         Translational activator of cytochrome c oxidase 1         4         0.68         0.01           COX14         Q96136         Cytochrome c oxidase assembly protein COX14         1         0.74         0.02           COA7         Q96BR5         Cytochrome c oxidase assembly protein COX14         1         0.74         0.03           SCO1         O75880         Protein SCO2 homolog, mitochondrial         2         0.87         0.01           SCO2         O43819         Protein SCO2 homolog, mitochondrial         2         0.87         0.01           SCO2         O43819         Protein SCO2 homolog, mitochondrial         2         1.14         0.01           SCO1         O75806         Protein SCO2 homolog, mitochondrial         2         1.34         0.01           SURF1         Q15526         Surfeit locus protein 1         3         1.55         0.00           SURF1         Q15526         Surfeit locus protein 1         2         0.62         0.01           ATP5MG         O75964         ATP synthase subunit 4         7         0.60         0.01           ATP5F1D<	COX19	Q49B96	Cytochrome c oxidase assembly protein COX19	3	0.38	0.00
TACO1       Q9BVV7       Mindenonarial import inner memorane translocase subunit 1mi21       5       0.062       0.01         TACO1       Q9BSH4       Translational activator of cytochrome c oxidase 1       4       0.688       0.01         COA7       Q96BR5       Cytochrome c oxidase assembly protein COX14       1       0.74       0.02         COA7       Q96BR5       Cytochrome c oxidase assembly protein COX14       1       0.74       0.02         SMIM20       Q8NSG0       Small integral membrane protein 20       1       0.84       0.03         SCO1       O75880       Protein SCO1 homolog, mitochondrial       2       0.87       0.01         SCO2       Q43819       Protein SCO2 homolog, mitochondrial       2       0.87       0.01         COX20       Q5R115       Cytochrome c oxidase assembly protein COX20, mitochondrial       2       1.34       0.01         SURF1       Q15526       Surfeit locus protein 1       3       1.55       0.00         SURF1       Q15526       Surfeit locus protein 1       7       0.49       0.03         ATP5MG       O75964       ATP synthase subunit entiochondrial       7       0.60       0.01         MT-ATP6       P00846       ATP synthase subunit entincohondrial	COXII	Q9Y6N1	Cytochrome c oxidase assembly protein COX11, mitochondrial	3	0.58	0.01
COX1       Q9B5114       Initiation of Cytochrome c oxidase assembly protein COX14       1       0.74       0.02         COX7       Q96B85       Cytochrome c oxidase assembly protein COX14       1       0.74       0.02         COX1       Q96B85       Cytochrome c oxidase assembly protein COX14       1       0.84       0.03         SC01       O75880       Protein SCO1 homolog, mitochondrial       2       0.87       0.01         SC02       O43819       Protein SCO2 homolog, mitochondrial       3       0.98       0.01         COX15       Q7KZN9       Cytochrome c oxidase assembly protein COX15 homolog       2       1.14       0.01         SUR1       Q15526       Surfeit locus protein 1       3       1.55       0.00         CV subunits         DMAC2L       Q99766       ATP synthase subunit s, mitochondrial       7       0.49       0.03         MT-ATP6       P00846       ATP synthase subunit delta, mitochondrial       3       0.68       0.00         MT-SPFID       P3049       ATP synthase subunit delta, mitochondrial       3       0.68       0.00         ATPSPB       P24539       ATP synthase subunit delta, mitochondrial       1       0.77       0.00         ATPSPD       O7	TIMM21	Q9BVV/	Translational activator of autochrome a avidesa 1	5	0.62	0.01
COAT         QMBRS         Cytochrome c oxidase assembly factor 7         1         0.71         0.00           SMIM20         Q8N5G0         Small integral membrane protein 20         1         0.84         0.03           SCO1         075880         Protein SCO1 homolog, mitochondrial         2         0.87         0.01           SCO2         043819         Protein SCO2 homolog, mitochondrial         3         0.98         0.01           COX20         Q5R15         Cytochrome c oxidase assembly protein COX20, mitochondrial         2         1.14         0.01           COX15         Q7KZN9         Cytochrome c oxidase assembly protein COX15 homolog         2         1.34         0.01           SURF1         Q15526         Surfeit locus protein 1         3         1.55         0.00           CV submits           DMAC2L         Q99766         ATP synthase subunit a, mitochondrial         7         0.60         0.01           MT-ATP6         P00846         ATP synthase subunit a, mitochondrial         3         0.68         0.00           ATPSHD         P3049         ATP synthase subunit a, mitochondrial         3         0.68         0.00           ATPSMF         P56134         ATP synthase subunit 1, mitochondrial         2	COX14	096136	Cytochrome c oxidase assembly protein COX14	4	0.08	0.01
SMIM20         Q8N5G0         Small integral membrane protein 20         1         0.84         0.03           SCO1         O75880         Protein SCO1 homolog, mitochondrial         2         0.87         0.01           SCO2         O43819         Protein SCO1 homolog, mitochondrial         2         1.14         0.01           COX20         Q5R115         Cytochrome c oxidase assembly protein COX20, mitochondrial         2         1.34         0.01           COX15         Q7KZN9         Cytochrome c oxidase assembly protein COX15 homolog         2         1.34         0.01           SURF1         Q15526         Surfeit locus protein 1         3         1.55         0.00           CV subunis           7         0.49         0.03           ATP5MG         O75964         ATP synthase subunit a, mitochondrial         7         0.60         0.01           MT-ATP6         P00846         ATP synthase subunit a, mitochondrial         3         0.68         0.00           ATP5MG         O75964         ATP synthase subunit b, mitochondrial         5         0.71         0.00           ATPSME         P56385         ATP synthase subunit b, mitochondrial         10         0.73         0.00           ATPSMF	COA7	096BR5	Cytochrome c oxidase assembly factor 7	4	0.81	0.00
SCO1 $075880$ Protein SCO1 homolog, mitochondrial2 $0.87$ $0.01$ SCO2 $043819$ Protein SCO2 homolog, mitochondrial3 $0.98$ $0.01$ COX20Q5R115Cytochrome c oxidase assembly protein COX20, mitochondrial2 $1.14$ $0.01$ COX15Q7KZN9Cytochrome c oxidase assembly protein COX15 homolog2 $1.34$ $0.01$ SURF1Q15526Surfeit locus protein 13 $1.55$ $0.00$ CV subunitsDMAC2LQ99766ATP synthase subunit s, mitochondrial7 $0.60$ $0.01$ MT-ATP6P00846ATP synthase subunit a, mitochondrial7 $0.60$ $0.01$ ATP5F1DP30049ATP synthase subunit a, mitochondrial3 $0.68$ $0.00$ ATP5MEP56385ATP synthase subunit e, mitochondrial5 $0.71$ $0.00$ ATP5MFP56134ATP synthase subunit f, mitochondrial13 $0.73$ $0.00$ ATP5MCP4439ATP synthase subunit f, mitochondrial1 $0.77$ $0.00$ ATP5MC3P48407ATP synthase subunit f, mitochondrial1 $0.77$ $0.00$ ATP5F1BP06576ATP synthase subunit beta, mitochondrial10 $0.79$ $0.00$ ATP5F1AP2505ATP synthase subunit d, mitochondrial10 $0.79$ $0.00$ ATP5F1BP06576ATP synthase subunit d, mitochondrial3 $0.98$ $0.00$ ATP5F1BP06576ATP synthase subunit d, mitochondrial3 $0$	SMIM20	Q8N5G0	Small integral membrane protein 20	1	0.84	0.03
SCO2         O43819         Protein SCO2 homolog, mitochondrial         3         0.98         0.01           COX20         Q5R115         Cytochrome c oxidase assembly protein COX20, mitochondrial         2         1.14         0.01           COX15         Q7KZN9         Cytochrome c oxidase assembly protein COX15 homolog         2         1.34         0.01           SURF1         Q15526         Surfeit locus protein 1         3         1.55         0.00           CV subunits           DMAC2L         Q99766         ATP synthase subunit s, mitochondrial         7         0.60         0.01           MT-ATP6         P00846         ATP synthase subunit a         2         0.62         0.01           MT-ATP6         P00846         ATP synthase subunit a         2         0.62         0.01           MT-SPID         P30049         ATP synthase subunit a, mitochondrial         3         0.68         0.00           ATPSME         P56385         ATP synthase subunit B, mitochondrial         13         0.73         0.00           ATPSPB         P24539         ATP synthase subunit C3, mitochondrial         11         0.77         0.00           ATPSTO         O75947         ATP synthase subunit C3, mitochondrial         1	SCO1	075880	Protein SCO1 homolog, mitochondrial	2	0.87	0.01
COX20         QSR115         Cytochrome c oxidase assembly protein COX20, mitochondrial         2         1.14         0.01           COX15         Q7KZN9         Cytochrome c oxidase assembly protein COX15 homolog         2         1.34         0.01           SURF1         Q15526         Surfeit locus protein 1         3         1.55         0.00           CV subunits           3         1.55         0.00           MAC2L         Q99766         ATP synthase subunit s, mitochondrial         7         0.60         0.01           MT-ATP6         P00846         ATP synthase subunit a, mitochondrial         7         0.62         0.01           ATP5MG         O75964         ATP synthase subunit a, mitochondrial         3         0.68         0.00           ATP5F1D         P30049         ATP synthase subunit a, mitochondrial         3         0.68         0.00           ATP5ME         P56385         ATP synthase subunit f, mitochondrial         13         0.73         0.00           ATP5MF         P56134         ATP synthase subunit C3, mitochondrial         11         0.77         0.00           ATP5PD         O75947         ATP synthase subunit C3, mitochondrial         1         0.77         0.00           ATP	SCO2	O43819	Protein SCO2 homolog, mitochondrial	3	0.98	0.01
COX15         Q7KZN9         Cytochrome c oxidase assembly protein COX15 homolog         2         1.34         0.01           SURF1         Q15526         Surfeit locus protein 1         3         1.55         0.00           CV subunits           3         1.55         0.00           CV subunits           7         0.49         0.03           ATP5MG         O75964         ATP synthase subunit g, mitochondrial         7         0.60         0.01           MT-ATP6         P00846         ATP synthase subunit a, mitochondrial         2         0.62         0.01           ATP5FID         P30049         ATP synthase subunit e, mitochondrial         3         0.68         0.00           ATP5PB         P24539         ATP synthase subunit B1, mitochondrial         13         0.73         0.00           ATP5PB         P24539         ATP synthase subunit C3, mitochondrial         11         0.75         0.00           ATP5PD         O75947         ATP synthase subunit 0, mitochondrial         1         0.77         0.00           ATP5PD         P48201         ATP synthase subunit C3, mitochondrial         1         0.77         0.00           ATP5F1B         P06576         ATP syntha	COX20	Q5RI15	Cytochrome c oxidase assembly protein COX20, mitochondrial	2	1.14	0.01
SURF1         Q15326         Surfeit locus protein 1         3         1.55         0.00           CV subunits         DMAC2L         Q99766         ATP synthase subunit s, mitochondrial         7         0.49         0.03           ATP5MG         O75964         ATP synthase subunit g, mitochondrial         7         0.60         0.01           MT-ATP6         P00846         ATP synthase subunit a         2         0.62         0.01           ATP5FID         P30049         ATP synthase subunit e, mitochondrial         3         0.68         0.00           ATP5FID         P30049         ATP synthase subunit e, mitochondrial         13         0.73         0.00           ATP5FID         P30747         ATP synthase subunit f, mitochondrial         13         0.73         0.00           ATP5FID         P30747         ATP synthase subunit G, mitochondrial         1         0.77         0.00           ATP5FID         O75947         ATP synthase subunit C3, mitochondrial         1         0.77         0.00           ATP5FIB         P06576         ATP synthase subunit anitochondrial         10         0.79         0.00           ATP5FIB         P06576         ATP synthase subunit anitochondrial         12         0.84         0.00	COX15	Q7KZN9	Cytochrome c oxidase assembly protein COX15 homolog	2	1.34	0.01
CV subunits         7         0.49         0.03           ATP5MG         O75964         ATP synthase subunit s, mitochondrial         7         0.60         0.01           MT-ATP6         P00846         ATP synthase subunit a         2         0.62         0.01           MT-ATP6         P00846         ATP synthase subunit delta, mitochondrial         3         0.68         0.00           ATP5FID         P30049         ATP synthase subunit delta, mitochondrial         5         0.71         0.00           ATP5ME         P56385         ATP synthase subunit delta, mitochondrial         13         0.73         0.00           ATP5MF         P56134         ATP synthase subunit f, mitochondrial         11         0.75         0.00           ATP5MF         P56134         ATP synthase subunit d, mitochondrial         1         0.77         0.00           ATP5MC3         P48201         ATP synthase subunit C3, mitochondrial         1         0.77         0.00           ATP5FIB         P06576         ATP synthase subunit beta, mitochondrial         2         0.78         0.00           ATP5FIB         P06576         ATP synthase subunit gamma, mitochondrial         10         0.79         0.00           ATP5FIC         P36542 <td< td=""><td>SURFI</td><td>Q15526</td><td>Surfeit locus protein 1</td><td>3</td><td>1.55</td><td>0.00</td></td<>	SURFI	Q15526	Surfeit locus protein 1	3	1.55	0.00
DMAC2L         Q99766         ATP synthase subunit s, mitochondrial         7         0.49         0.03           ATP5MG         O75964         ATP synthase subunit g, mitochondrial         7         0.60         0.01           MT-ATP6         P00846         ATP synthase subunit a, mitochondrial         2         0.62         0.01           ATP5FID         P30049         ATP synthase subunit c, mitochondrial         3         0.68         0.00           ATP5FME         P56385         ATP synthase subunit c, mitochondrial         5         0.71         0.00           ATP5ME         P56134         ATP synthase subunit f, mitochondrial         13         0.73         0.00           ATP5MF         P56134         ATP synthase subunit d, mitochondrial         2         0.74         0.00           ATP5MF         P56134         ATP synthase subunit C3, mitochondrial         1         0.77         0.00           ATP5MC3         P48201         ATP synthase subunit C3, mitochondrial         1         0.77         0.00           ATP5FIB         P06576         ATP synthase subunit and mitochondrial         10         0.79         0.00           ATP5F1A         P25705         ATP synthase subunit and mitochondrial         10         0.79         0.00 </td <td>CV subunits</td> <td></td> <td></td> <td></td> <td></td> <td></td>	CV subunits					
ATP 5MG       O75964       ATP synthase subunit g, mitochondrial       7       0.60       0.01         MT-ATP6       P00846       ATP synthase subunit a       2       0.62       0.01         ATP5F1D       P30049       ATP synthase subunit delta, mitochondrial       3       0.68       0.00         ATP5FME       P56385       ATP synthase subunit e, mitochondrial       5       0.71       0.00         ATP5PB       P24539       ATP synthase subunit f, mitochondrial       13       0.73       0.00         ATP5MF       P56134       ATP synthase subunit d, mitochondrial       2       0.74       0.00         ATP5MD       O75947       ATP synthase subunit d, mitochondrial       1       0.75       0.00         ATP5F1B       P06576       ATP synthase subunit O, mitochondrial       25       0.78       0.00         ATP5F1A       P25705       ATP synthase subunit on, mitochondrial       10       0.79       0.00         ATP5F1C       P36542       ATP synthase subunit gamma, mitochondrial       12       0.84       0.00         MTP5F1A       P25705       ATP synthase subunit gamma, mitochondrial       1       0.94       0.01         ATP5F1C       P36542       ATP synthase subunit epsilon, mitochondrial <t< td=""><td>DMAC2L</td><td>Q99766</td><td>ATP synthase subunit s, mitochondrial</td><td>7</td><td>0.49</td><td>0.03</td></t<>	DMAC2L	Q99766	ATP synthase subunit s, mitochondrial	7	0.49	0.03
MT-A1P6       P00846       ATP synthase subunit a       2       0.62       0.01         ATP5F1D       P30049       ATP synthase subunit delta, mitochondrial       3       0.68       0.00         ATP5F1D       P30049       ATP synthase subunit delta, mitochondrial       5       0.71       0.00         ATP5PB       P24539       ATP synthase subunit f, mitochondrial       13       0.73       0.00         ATP5MF       P56134       ATP synthase subunit f, mitochondrial       2       0.74       0.00         ATP5MD       O75947       ATP synthase subunit f, mitochondrial       1       0.75       0.00         ATP5MC3       P48201       ATP synthase subunit C3, mitochondrial       1       0.77       0.00         ATP5F1B       P06576       ATP synthase subunit C3, mitochondrial       10       0.79       0.00         ATP5F1A       P25705       ATP synthase subunit aph, mitochondrial       10       0.79       0.00         ATP5F1C       P36542       ATP synthase subunit gamma, mitochondrial       12       0.84       0.00         MT-ATP8       P03928       ATP synthase subunit gamma, mitochondrial       3       0.98       0.00         ATP5F1E       P56381       ATP synthase subunit epsilon, mitochondrial	ATP5MG	075964	ATP synthase subunit g, mitochondrial	7	0.60	0.01
ATPSFID       P30049       ATP synthase subunit defta, mitochondrial       5       0.08       0.00         ATP5ME       P56385       ATP synthase subunit e, mitochondrial       13       0.73       0.00         ATP5MF       P24539       ATP synthase subunit f, mitochondrial       13       0.73       0.00         ATP5MF       P56134       ATP synthase subunit f, mitochondrial       11       0.75       0.00         ATP5PD       075947       ATP synthase subunit d, mitochondrial       11       0.77       0.00         ATP5FIB       P06576       ATP synthase subunit beta, mitochondrial       1       0.77       0.00         ATP5F1B       P06576       ATP synthase subunit beta, mitochondrial       10       0.79       0.00         ATP5F1A       P25705       ATP synthase subunit alpha, mitochondrial       10       0.79       0.00         ATP5F1C       P36542       ATP synthase subunit gamma, mitochondrial       12       0.84       0.00         MT-ATP8       P03928       ATP synthase subunit epsilon, mitochondrial       3       0.98       0.00         ATP5F1E       P56381       ATP synthase subunit epsilon, mitochondrial       3       0.98       0.00         ATP5F1E       P56381       ATP synthase protein 8<	MT-ATP6	P00846	ATP synthase subunit a	2	0.62	0.01
ATPSME       F36353       ATP synthase subunit e, initochondrial       13       0.71       0.00         ATP5PB       P24539       ATP synthase F(0) complex subunit B1, mitochondrial       13       0.73       0.00         ATP5MF       P56134       ATP synthase subunit f, mitochondrial       2       0.74       0.00         ATP5MD       O75947       ATP synthase subunit d, mitochondrial       11       0.75       0.00         ATP5MC3       P48201       ATP synthase subunit C3, mitochondrial       1       0.77       0.00         ATP5F1B       P06576       ATP synthase subunit 0, mitochondrial       10       0.79       0.00         ATP5F1A       P25705       ATP synthase subunit 0, mitochondrial       10       0.79       0.00         ATP5F1C       P36542       ATP synthase subunit gamma, mitochondrial       12       0.84       0.00         MT-ATP8       P03928       ATP synthase subunit epsilon, mitochondrial       3       0.98       0.00         ATP5F1E       P56381       ATP synthase subunit epsilon, mitochondrial       3       0.98       0.00         ATP5F1F1       Q9U112       ATPase inhibitor, mitochondrial       4       1.16       0,01         ATP5FF7       P18859       ATP synthase mitochondrial<	ATPSFID	P30049	A I P synthase subunit delta, mitochondrial	5	0.68	0.00
ATP5MF       P56134       ATP synthase subunit f, mitochondrial       10       0.75       0.00         ATP5PD       O75947       ATP synthase subunit d, mitochondrial       11       0.75       0.00         ATP5PD       O75947       ATP synthase subunit d, mitochondrial       11       0.77       0.00         ATP5PD       O75947       ATP synthase subunit C3, mitochondrial       1       0.77       0.00         ATP5F1B       P06576       ATP synthase subunit beta, mitochondrial       25       0.78       0.00         ATP5F1B       P06576       ATP synthase subunit 0, mitochondrial       10       0.79       0.00         ATP5F1B       P06576       ATP synthase subunit 1, mitochondrial       10       0.79       0.00         ATP5F1A       P25705       ATP synthase subunit apha, mitochondrial       10       0.79       0.00         ATP5F1C       P36542       ATP synthase subunit gamma, mitochondrial       12       0.84       0.00         MT-ATP8       P03928       ATP synthase subunit epsilon, mitochondrial       1       0.94       0.01         ATP5F1E       P56381       ATP synthase subunit epsilon, mitochondrial       3       0.98       0.00         ATP5F1F       P18859       ATP synthase-coupling factor	ATP5PR	P24539	ATP synthase $F(0)$ complex subunit B1 mitochondrial	13	0.71	0.00
ATP5PD       O75947       ATP synthase subunit d, mitochondrial       11       0.75       0.00         ATP5MC3       P48201       ATP synthase F(0) complex subunit C3, mitochondrial       1       0.77       0.00         ATP5F1B       P06576       ATP synthase subunit beta, mitochondrial       25       0.78       0.00         ATP5F1B       P06576       ATP synthase subunit O, mitochondrial       10       0.79       0.00         ATP5F1A       P25705       ATP synthase subunit alpha, mitochondrial       36       0.79       0.00         ATP5F1C       P36542       ATP synthase subunit gamma, mitochondrial       12       0.84       0.00         MT-ATP8       P03928       ATP synthase protein 8       1       0.94       0.01         ATP5F1E       P56381       ATP synthase subunit epsilon, mitochondrial       3       0.98       0.00         ATP5F1F       Q9UII2       ATPase inhibitor, mitochondrial       4       1.16       0,01         ATP5FF       P18859       ATP synthase mitochondrial       4       1.18       0.00         CV assembly factors       T       2       0.86       0.02       2       0.86       0.02         FMC1       Q96HJ9       Protein FMC1 homolog       2	ATP5MF	P56134	ATP synthase subunit f. mitochondrial	2	0.74	0.00
ATP5MC3       P48201       ATP synthase F(0) complex subunit C3, mitochondrial       1       0.77       0.00         ATP5F1B       P06576       ATP synthase subunit beta, mitochondrial       25       0.78       0.00         ATP5F1B       P06576       ATP synthase subunit O, mitochondrial       10       0.79       0.00         ATP5PO       P48047       ATP synthase subunit O, mitochondrial       10       0.79       0.00         ATP5F1A       P25705       ATP synthase subunit alpha, mitochondrial       36       0.79       0.00         ATP5F1C       P36542       ATP synthase subunit gamma, mitochondrial       12       0.84       0.00         MT-ATP8       P03928       ATP synthase protein 8       1       0.94       0.01         ATP5F1E       P56381       ATP synthase subunit epsilon, mitochondrial       3       0.98       0.00         ATP5F1F1       Q9UII2       ATPase inhibitor, mitochondrial       4       1.16       0,01         ATP5FF       P18859       ATP synthase-coupling factor 6, mitochondrial       4       1.18       0.00         CV assembly factors       Image: protein FMC1 homolog       2       0.86       0.02         FMC1       Q96HJ9       Protein FMC1 homolog       2       0.86	ATP5PD	075947	ATP synthase subunit d, mitochondrial	11	0.75	0.00
ATP5F1B       P06576       ATP synthase subunit beta, mitochondrial       25       0.78       0.00         ATP5PO       P48047       ATP synthase subunit 0, mitochondrial       10       0.79       0.00         ATP5F1A       P25705       ATP synthase subunit alpha, mitochondrial       36       0.79       0.00         ATP5F1C       P36542       ATP synthase subunit gamma, mitochondrial       12       0.84       0.00         MT-ATP8       P03928       ATP synthase protein 8       1       0.94       0.01         ATP5F1E       P56381       ATP synthase subunit epsilon, mitochondrial       3       0.98       0.00         ATP5F1F       Q9UII2       ATPase inhibitor, mitochondrial       4       1.16       0,01         ATP5FF       P18859       ATP synthase-coupling factor 6, mitochondrial       4       1.18       0.00         CV assembly factors         4       1.18       0.00         FMC1       Q96HJ9       Protein FMC1 homolog       2       0.86       0.02         ATPAF1       Q5TC12       ATP synthase mitochondrial F1 complex assembly factor 1       5       0.93       0.01	ATP5MC3	P48201	ATP synthase F(0) complex subunit C3, mitochondrial	1	0.77	0.00
ATP5POP48047ATP synthase subunit O, mitochondrial100.790.00ATP5F1AP25705ATP synthase subunit alpha, mitochondrial360.790.00ATP5F1CP36542ATP synthase subunit gamma, mitochondrial120.840.00MT-ATP8P03928ATP synthase protein 810.940.01ATP5F1EP56381ATP synthase subunit epsilon, mitochondrial30.980.00ATP5F1FQ9UII2ATPase inhibitor, mitochondrial41.160,01ATP5FFP18859ATP synthase-coupling factor 6, mitochondrial41.180.00CV assembly factorsATPAF2Q8N5M1ATP synthase mitochondrial F1 complex assembly factor 250.600.03FMC1Q96HJ9Protein FMC1 homolog20.860.02ATPAF1Q5TC12ATP synthase mitochondrial F1 complex assembly factor 150.930.01	ATP5F1B	P06576	ATP synthase subunit beta, mitochondrial	25	0.78	0.00
ATP5F1AP25705ATP synthase subunit alpha, mitochondrial360.790.00ATP5F1CP36542ATP synthase subunit gamma, mitochondrial120.840.00MT-ATP8P03928ATP synthase protein 810.940.01ATP5F1EP56381ATP synthase subunit epsilon, mitochondrial30.980.00ATP5F1FQ9UII2ATPase inhibitor, mitochondrial41.160,01ATP5FFP18859ATP synthase-coupling factor 6, mitochondrial41.180.00CV assembly factorsATPAF2Q8N5M1ATP synthase mitochondrial F1 complex assembly factor 250.600.03FMC1Q96HJ9Protein FMC1 homolog20.860.02ATPAF1Q5TC12ATP synthase mitochondrial F1 complex assembly factor 150.930.01	ATP5PO	P48047	ATP synthase subunit O, mitochondrial	10	0.79	0.00
A1P5F1CP36542ATP synthase subunit gamma, mitochondrial120.840.00MT-ATP8P03928ATP synthase protein 810.940.01ATP5F1EP56381ATP synthase subunit epsilon, mitochondrial30.980.00ATP5IF1Q9UII2ATPase inhibitor, mitochondrial41.160,01ATP5FFP18859ATP synthase-coupling factor 6, mitochondrial41.180.00CV assembly factorsATPAF2Q8N5M1ATP synthase mitochondrial F1 complex assembly factor 250.600.03FMC1Q96HJ9Protein FMC1 homolog20.860.02ATPAF1Q5TC12ATP synthase mitochondrial F1 complex assembly factor 150.930.01	ATP5F1A	P25705	ATP synthase subunit alpha, mitochondrial	36	0.79	0.00
M1-A1P8P03928A1P synthase protein 810.940.01ATP5F1EP56381ATP synthase subunit epsilon, mitochondrial30.980.00ATP5IF1Q9UII2ATPase inhibitor, mitochondrial41.160,01ATP5PFP18859ATP synthase-coupling factor 6, mitochondrial41.180.00CV assembly factorsATPAF2Q8N5M1ATP synthase mitochondrial F1 complex assembly factor 250.600.03FMC1Q96HJ9Protein FMC1 homolog20.860.02ATPAF1Q5TC12ATP synthase mitochondrial F1 complex assembly factor 150.930.01	ATP5F1C	P36542	ATP synthase subunit gamma, mitochondrial	12	0.84	0.00
ATPSTEF50561ATP synthase subulif epsilon, millochondrial50.980.00ATP51F1Q9UII2ATPase inhibitor, mitochondrial41.160,01ATP5PFP18859ATP synthase-coupling factor 6, mitochondrial41.180.00CV assembly factorsATPAF2Q8N5M1ATP synthase mitochondrial F1 complex assembly factor 250.600.03FMC1Q96HJ9Protein FMC1 homolog20.860.02ATPAF1Q5TC12ATP synthase mitochondrial F1 complex assembly factor 150.930.01	MI-ATP8	P03928	A I P synthase protein 8 A TP synthase subunit engilen mitacher driel	1	0.94	0.01
ATP5PFP18859ATP synthase-coupling factor 6, mitochondrial41.100,01CV assembly factors41.180.00CV assembly factors50.600.03FMC1Q96HJ9Protein FMC1 homolog20.860.02ATPAF1Q5TC12ATP synthase mitochondrial F1 complex assembly factor 150.930.01	ATP5FIE ATP5IF1	0011112	ATF synthase subunit epsilon, intochondrial	5 Д	0.98	0.00
CV assembly factorsATPAF2Q8N5M1ATP synthase mitochondrial F1 complex assembly factor 250.600.03FMC1Q96HJ9Protein FMC1 homolog20.860.02ATPAF1Q5TC12ATP synthase mitochondrial F1 complex assembly factor 150.930.01	ATP5PF	P18859	ATP synthase-coupling factor 6, mitochondrial	4	1.18	0.00
CV assembly factorsATPAF2Q8N5M1ATP synthase mitochondrial F1 complex assembly factor 250.600.03FMC1Q96HJ9Protein FMC1 homolog20.860.02ATPAF1Q5TC12ATP synthase mitochondrial F1 complex assembly factor 150.930.01			- 10 - 7		-	- 14
ATTAT2Q0100MTATT synthase introchondrial F1 complex assembly factor 250.600.03FMC1Q96HJ9Protein FMC1 homolog20.860.02ATPAF1Q5TC12ATP synthase mitochondrial F1 complex assembly factor 150.930.01	CV assembly f	factors	ATD synthese mitschandrial El samplay assembly faster 2	5	0.60	0.02
ATPAF1 Q5TC12 ATP synthase mitochondrial F1 complex assembly factor 1 5 0.93 0.01	FMC1	O96HI9	Protein FMC1 homolog	3 2	0.86	0.03
	ATPAF1	Q5TC12	ATP synthase mitochondrial F1 complex assembly factor 1	5	0.93	0.01

FDR values marked in grey are not significant (P>0.05); C, complex

Gene Symbol	UniProt Accession	Description	Unique Peptides	log2 FC	FDR
Fatty Acid Oxi	dation (FAO	)			
ACADS	P16219	Short-chain specific acyl-CoA dehydrogenase, mitochondrial	12	-1.99	0.01
ETFDH	Q16134	Electron transfer flavoprotein-ubiquinone oxidoreductase, mitochondrial	15	-1.08	0.00
ACADSB	P45954	Short/branched chain specific acyl-CoA dehydrogenase, mitochondrial	7	-1.04	0.01
ACADM	P11310	Medium-chain specific acyl-CoA dehydrogenase, mitochondrial	15	-0.88	0.05
ACSS1	Q9NUB1	Acetyl-coenzyme A synthetase 2-like, mitochondrial	9	-0.08	0.84
ACOT11	Q8WXI4	Acyl-coenzyme A thioesterase 11	1	0.25	0.60
ACSF2	Q96CM8	Medium-chain acyl-CoA ligase ACSF2, mitochondrial	11	0.28	0.02
CROT	Q9UKG9	Peroxisomal carnitine O-octanoyltransferase	1	0.28	0.54
ACADVL	P49748	Very long-chain specific acyl-CoA dehydrogenase, mitochondrial	37	0.36	0.25
CRAT	P43155	Carnitine O-acetyltransferase	23	0.41	0.03
ECHS1	P30084	Enoyl-CoA hydratase, mitochondrial	16	0.54	0.01
MMUT	P22033	Methylmalonyl-CoA mutase, mitochondrial	8	0.56	0.03
ACAT1	P24752	Acetyl-CoA acetyltransferase, mitochondrial	22	0.58	0.03
ECI1	P42126	Enoyl-CoA delta isomerase 1, mitochondrial	8	0.61	0.01
ACACB	000763	Acetyl-CoA carboxylase 2 O	10	0.74	0.00
DECR1	Q16698	2,4-dienoyl-CoA reductase [(3E)-enoyl-CoA-producing], mitochondrial	14	0.89	0.00
HADH	Q16836	Hydroxyacyl-coenzyme A dehydrogenase, mitochondrial	12	0.94	0.01
MCEE	Q96PE7	Methylmalonyl-CoA epimerase, mitochondrial	5	1.00	0.01
ETFB	P38117	Electron transfer flavoprotein subunit beta	16	1.10	0.00
SLC25A20	043772	Mitochondrial carnitine/acylcarnitine carrier protein	8	1.03	0.01
HSD17B10	Q99714	3-hydroxyacyl-CoA dehydrogenase type-2	10	1.04	0.00
CPT1B	Q92523	Carnitine O-palmitoyltransferase 1, muscle isoform	23	1.13	0.01
ETFA	P13804	Electron transfer flavoprotein subunit alpha, mitochondrial	11	1.14	0.00
ECI2	075521	Enoyl-CoA delta isomerase 2	10	1.16	0.00
CPT2	P23786	Carnitine O-palmitoyltransferase 2, mitochondrial	23	1.17	0.01
ACSL1	P33121	Long-chain-fatty-acidCoA ligase 1	35	1.20	0.00
PCCA	P05165	Propionyl-CoA carboxylase alpha chain, mitochondrial	18	1.31	0.01
PCCB	P05166	Propionyl-CoA carboxylase beta chain, mitochondrial	12	1.33	0.01
ACAA2	P42765	3-ketoacyl-CoA thiolase, mitochondrial	21	1.34	0.00
HADHB	P55084	Trifunctional enzyme subunit beta, mitochondrial	27	1.73	0,00
HADHA	P40939	Trifunctional enzyme subunit alpha, mitochondrial	40	1.78	0.00
CPT1A	P50416	Carnitine O-palmitoyltransferase 1, liver isoform	4	2.17	0.00
Citric acid cycl	e (TCA)				
DLD	P09622	Dihydrolipoyl dehydrogenase, mitochondrial	14	-1.15	0.01
OGDH	Q02218	2-oxoglutarate dehydrogenase complex component E1	42	-0.49	0.03
PC	P11498	Pyruvate carboxylase, mitochondrial	1	0.35	0.03
SLC25A11	Q02978	Mitochondrial 2-oxoglutarate/malate carrier protein	13	0.37	0.03
L2HGDH	Q9H9P8	L-2-hydroxyglutarate dehydrogenase, mitochondrial	7	0.05	0.80
ACLY	P53396	ATP-citrate synthase	6	0.26	0.29
ME2	P23368	NAD-dependent malic enzyme, mitochondrial	4	0.40	0.07
IDH2	P48735	Isocitrate dehydrogenase [NADP], mitochondrial	26	0.51	0.01
SUCLA2	Q9P2R7	SuccinateCoA ligase [ADP-forming] subunit beta, mitochondrial	23	0.52	0.01
MPC2	O95563	Mitochondrial pyruvate carrier 2	1	0.62	0.14
MDH2	P40926	Malate dehydrogenase, mitochondrial	19	0.64	0.01
MPC1	Q9Y5U8	Mitochondrial pyruvate carrier 1	1	0.69	0.04
DLST	P36957	Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate	14	0.73	0.01
SUCLG1	P53597	SuccinateCoA ligase [ADP/GDP-forming] subunit alpha, mitochondrial	10	0.76	0.00
ABHD11	Q8NFV4	sn-1-specific diacylglycerol lipase ABHD11	3	0.79	0.00
CS	O75390	Citrate synthase, mitochondrial	16	0.79	0.00
FAHD1	Q6P587	Acylpyruvase FAHD1, mitochondrial	7	0.85	0.00
IDH3B	O43837	Isocitrate dehydrogenase [NAD] subunit beta, mitochondrial	11	0.88	0.02
FH	P07954	Fumarate hydratase, mitochondrial	20	0.90	0.00
ACO2	Q99798	Aconitate hydratase, mitochondrial	41	0.94	0.00
IDH3G	P51553	Isocitrate dehydrogenase [NAD] subunit gamma, mitochondrial	9	0.97	0.01
IDH3A	P50213	Isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial	16	0.99	0.01
ME3	Q16798	NADP-dependent malic enzyme, mitochondrial	5	1.00	0.00
SUCLG2	Q96I99	SuccinateCoA ligase [GDP-forming] subunit beta, mitochondrial	19	1.56	0.00
PCK2	Q16822	Phosphoenolpyruvate carboxykinase [GTP], mitochondrial	8	3.10	0.00

Supplementary Table 5. List of proteins detected in fatty acid oxidation and citric acid cycle in the proteomic
analysis

FDR values marked in grey are not significant (P>0.05)



**Supplementary Fig 5.** Western blot analysis. The overall pattern showed a reduced amount of Complex I, II and IV, but no reduction of Complex III and V. The membranes were cut into pieces according to the size of the corresponding proteins to be able to incubate several antibodies on one blotted membrane. This was done for antibodies that are well-known to only show a band of correct molecular size. The figure of the western blot result is arranged from four agarose gels with equal amounts of loaded proteins derived from a single concentration measurement. L, Ladder; C, control; DC, disease control; (C and DC are specified in Supplementary Table 2); P, patients; MHC, Myosin heavy chain, Gel A and C, antibodies for ATPB, MT-CO1, NDUFB8, Gel B and D antibodies for UQCRC1, VDAC1, SDHB

#### Pharmocogenetic analysis

Sertraline is metabolized by CYP enzymes and pharmocogenetic studies suggest that *CYP2C19* is the major metabolic enzyme. Since some variants are reported to affect the enzyme activity we analyzed the presence of these variants in our patients (star alleles \*). We included 11 variants in our analysis (Supplementary Table 6). We identified two of the variants in 6 of our patients, CYP2C19\*2 detected in 4 and CYP2C19\*17 in 2. Both variants are common in the population with more than 20 000 homozygous individuals detected for each variant in the gnomAD database.

Allele	cDNA	Protein change	Effect on enzyme activity	dbSNP rsID	gnomAD v4.1.0	11 patients 22 alleles
*1	None (wt)		Normal (extensive) activity			10/11 15/22
*2	c.681G>A	p.P227P	No activity	rs4244285	234686/1464646ª 1.60e-1 <sup>b</sup> 20742 <sup>c</sup>	4/11 5/22 <sup>d</sup>
*3	c.636G>A	p.W212*	No activity	rs4986893	4750/1613588 <sup>a</sup> 0.002944 <sup>b</sup> 214 <sup>c</sup>	0/22
*4	c.1A>G	p.M1?	No activity	rs28399504	3866/1613130ª 2.40e-3 <sup>b</sup> 16 <sup>c</sup>	0/22
*5	c.1297C>T	p.R433W	No activity	rs56337013	28/1613634 <sup>a</sup> 1.74e-5 <sup>b</sup> 0 <sup>c</sup>	0/22
*6	c.395G>A	p.R132Q	No activity	rs72552267	489/1614044 <sup>a</sup> 3.03e-4 <sup>b</sup> 1 <sup>c</sup>	0/22
*7	c.819+2T>A	splice	No activity	rs72558186	3/1535118ª 1.95e-6 <sup>b</sup> 0 <sup>c</sup>	0/22
*8	c.358T>C	p.W120R	No activity	rs41291556	3867/1614036 <sup>a</sup> 2.40e-3 <sup>b</sup> 12 <sup>c</sup>	0/22
*9	c.431G>A	p.R144H	Decreased activity	rs17884712	1141/1614010 <sup>a</sup> 7.07e-4 <sup>b</sup> 7 <sup>c</sup>	0/22
*10	c.680C>T	p.P227L	Decreased activity	rs6413438	354/1471456 <sup>a</sup> 2.41e-4 <sup>b</sup> 1 <sup>c</sup>	0/22
*17	c806C>T	promotor	Enhanced activity	rs12248560	30385/151940 <sup>a</sup> 0.2000 <sup>b</sup> 3261 <sup>c</sup>	2/11 2/22
*35	c.332-23A>G <sup>e</sup>	splice	No activity	rs12769205	266140/1612890ª 1.65e-1 <sup>b</sup> 24492°	0/22

Supplementary Table 6. Genetic analyses of individual Star alleles\* for CYP2C19 with effect on enzyme activity

Included Star alleles\* based on https://www.mayocliniclabs.com/test-catalog/overview/610043#Clinical-and-Interpretive, *CYP2C19*; NM\_000769.1

<sup>a</sup> allele count/total allele number, <sup>b</sup> allele frequency, <sup>c</sup> number of homozygous, <sup>d</sup> together with c.332-23A>G,

<sup>e</sup> in the absence of c.681G>A