Supplementary Materials: The Complexity of Mitochondrial Complex IV: An Update of Cytochrome *c* Oxidase Biogenesis in Plants

Natanael Mansilla, Sofia Racca, Diana E. Gras, Daniel H. Gonzalez and Elina Welchen

Table S1. COX subunits and assembly factors in *Arabidopsis thaliana*.

Mitochondria-Encoded Catalytic-Core Subunits

	AGI	Prot ID	Protein Name	Description	Experimental Evidence [a]	PTMS [b]	PPI [c]	Ref. [d]
COX1	ATMG01360	P60620	Cytochrome *c* oxidase subunit 1.	COX is the component of the respiratory chain that catalyzes the reduction of oxygen to water. Subunits 1–3 form the functional core of the enzyme complex. Electrons originating in CYTc are transferred via the Cu_A center of COX2 and heme *a* of subunit 1 to the bimetallic center formed by heme a_3 and Cu_B.	MS [1]	NR	NR	[2]
COX2	ATMG00160	P93285	Cytochrome *c* oxidase subunit 2.		MS [3–9]	NR	NR	[2,10]
COX3	ATMG00730	P92514	Cytochrome *c* oxidase subunit 3.		MS [1]	NR	NR	[2]

Nuclear-Encoded Structural Subunits

	AGI	Prot ID	Protein Name	Description	Experimental Evidence [a]	PTMS [b]	PPI [c]	Ref. [d]
COX5b-1	AT3G15640	Q9LW15	Cytochrome *c* oxidase subunit 5b-1.	Nuclear-coded COX subunit.	MS [1,3–9] TP: 1-55 [11]	P-3 [12,13]	AT3G02150 [14]	[15–18]
COX5b-2	AT1G80230	Q9SSB8	Cytochrome *c* oxidase subunit 5b-2.	Nuclear-coded COX subunit.	MS [1,3–9] TP: 1-54 [11]	Ubi-78 [19]	NR	[15,16,20]
COX5b-3	AT1G52710	Q9SSS5	Putative cytochrome *c* oxidase subunit 5b-3.	Rubredoxin-like superfamily protein; nuclear-coded COX subunit.	Mitochondrion: 1.0 [21]	NR	NR	NR
COX5c-1	AT2G47380	O22912	Cytochrome *c* oxidase subunit 5c-1.	Nuclear-coded COX subunit.	MS [1,4,6,9,10]	NR	NR	[10,22–24]
COX5c-2	AT3G62400	Q9LZQ0	Cytochrome *c* oxidase subunit 5c-2.	Nuclear-coded COX subunit.	MS [9]	NR	NR	[22–24]
COX5c-3	AT5G61310	Q9FLK2	Probable cytochrome *c* oxidase subunit 5c-3.	Nuclear-coded COX subunit.	MS [9]	NR	NR	[22–24]
COX6a	AT4G37830	Q9T070	Cytochrome *c* oxidase subunit 6a.	Nuclear-coded COX subunit.	FP [25] MS [1,4,9,10] TP: 1-36 [26]	P-1 [12]	NR	[27]
COX6b-1	AT1G22450	Q9S7L9	Cytochrome *c* oxidase subunit 6b-1.	Nuclear-coded COX subunit.	MS [4,5,7–9,28]	N-Ace: 23, 160 [28,29] DIS 137-169, 147-158 [26]	AT5G35750 [30]	[10,27,31–33]
COX6b-2	AT5G57815	Q94SL0	Cytochrome *c* oxidase subunit 6b-2.	Nuclear-coded COX subunit.	Mitochondrion: 1.0 [21]	NR DIS 25-57, 35-46 [26]	NR	[31,33]
COX6b-3	AT4G28060	Q9SUD3	Cytochrome *c* oxidase subunit 6b-3	Nuclear-coded COX subunit.	MS [8–10]	NR	NR	[31,33]

COX6b-4	AT1G32710	Q9LPJ2	Putative cytochrome *c* oxidase subunit 6b-4.	COX subunit VIb family protein.	Mitochondrion: 1.0 [21]	DIS 74-106, 84-95 [26]	NR	NR
COX-X1	AT5G27760	Q8LG60	Hypoxia-responsive family protein (ATHIG2)	Integral component of the IMM, as a part of Complex IV.	MS [1,6,9]	NR	AT1G35670 [34]	[35]
COX-X2-1	AT4G00860	Q38842	ATOZI1	Putative pathogenesis-related protein induced in response to ozone, *Pseudomonas* strains and ROS.	MS [1,4–9]	UBI-76 [19]	NR	NR
COX-X2-2	AT1G01170	Q2HIQ2	Ozone-responsive stress-like protein (DUF1138)	Integral membrane component, involved in stress response.	MS [8–10]	NR	NR	NR
COX-X3	AT1G72020	Q9C7G5	TonB-dependent heme receptor A	Integral membrane component.	MS [1]	NR	NR	NR
COX-X4	AT4G21105	Q944S8	Cytochrome c oxidase/electron carrier	Integral membrane component.	MS [1,8–10]	UBI-2,16 [19]	AT3G57040 [36]	NR
COX-X5	AT3G43410	Q9M178	F-box/LRR protein.	Protein of unknown function.	MS [1,4]	NR	NR	NR
COX-X6	AT2G16460	Q9SIV6	Coiled-coil 90B-like protein (DUF1640)	Protein of unknown function (DUF1640)	MS [1,4,6,7–9,10,37] TP: 1-43 [26]	NR	NR	NR

COX Assembly Factors

Membrane Insertion and Processing of Catalytic Core Subunits

	AGI	**Prot ID**	**Protein Name**	**Description**	**Experimental Evidence** [a]	**PTMS** [b]	**PPI** [c]	**Ref.** [d]
OXA1	AT5G62050	Q42191	IMM protein OXA1 (Oxidase assembly 1 protein).	Membrane insertion of COX subunits; homologue of yeast oxidase assembly 1 (Oxa1), essential factor for protein sorting and assembly into membranes, essential for COX assembly and activity.	FP [38] MS [6,9]	NR	NR	[39]
OXA1L	AT2G46470	Q9SKD3	IMM protein OXA1-like.	Probably required for the insertion of integral membrane proteins into the IMM.	MS [6,9] TP: 1-22 [26]	NR	NR	NR
Peptidase S24/S26A/S26B/S26C family protein	AT1G23465	Q5BIV4	Peptidase S24/S26A/S26B/S26C family protein.	IMM peptidase complex; serine-type peptidase activity.	Mitochondrion: 1.0 [21]	NR	NR	NR
	AT1G53530	Q6NLT8			MS [9,37]	NR	NR	NR
	AT1G29960	Q67XF2			MS [9]	NR	NR	NR
MYB3R-3	AT3G08980	Q9S724			Mitochondrion: 1.00 [21]	NR	NR	[26]

Heme A Biosynthesis and Insertion

	AGI	Prot ID	Protein Name	Description	Experimental evidence [a]	PTMS [b]	PPI [c]	Ref. [d]
COX10	AT2G44520	O64886	Protoheme IX farnesyltransferase, mitochondrial.	Heme O synthase. Converts protoheme IX and farnesyl diphosphate to heme O. Essential protein for COX assembly and activity.	FP [40] MS [37] TP: 1-33 [26]	NR	NR	[40]
COX15	AT5G56090	Q9FKT8	Cytochrome *c* oxidase 15.	Involved in the biosynthesis of heme A, oxidation of heme O methyl to formyl; transcriptionally increased after treatment with rotenone.	MS [7,9]	NR	NR	NR
MFDX1	AT4G05450	Q9M0V0	Adrenodoxin-like protein 1.	Collaborates with COX15 in heme O oxidation. Associates in vitro with the adrenodoxin reductase MFDR to form an efficient low	FP [41] MS [8] TP: 1-35 [26]	NR	NR	[41,42]

MFDX2	AT4G21090	Q8S904	Adrenodoxin-like protein 2.	potential electron transfer chain that is able to reduce CYTc.	FP [41] TP: 1-74 [26]	UBI-217 [19]	NR	NR
MDFR	AT4G32360	Q8W3L1	Mitochondrial ferredoxin reductase.	Associates *in vitro* with the adrenodoxin-like protein MFDX1 to form an efficient low potential electron transfer chain that is able to reduce CYTc.	FP [41] MS [6,9] TP: 1-14 [26]	NR	NR	[41,42]
SURF1-1	AT3G17910	Q9SE51	SURFEIT 1	Similar to human SURF1 which is known to be involved in COX assembly. Catalyzes an assembly step involving COX1; proposed to participate in heme A delivery.	MS [4,6,7,9,10]	NR	NR	NR
SURF1-2	AT1G48510	Q9LP74	Surfeit locus 1 cytochrome c oxidase biogenesis protein.	Probably involved in the biogenesis of the COX complex.	Mitochondria: 1.0 [21]	NR	AT1G76310 AT3G10525 [43]	NR
				Coper Trafficking and Insertion				
	AGI	**Prot ID**	**Protein Name**	**Description**	**Experimental Evidence** [a]	**PTMS** [b]	**PPI** [c]	**Ref.** [d]
HCC1	AT3G08950	Q8VYP0	Electron transport SCO1.	Homologue of the copper chaperone Sco1 from the yeast *S. cerevisiae*. SCO1 encodes a mitochondrial protein that is essential for COX assembly. Thought to play a role in cellular copper homeostasis, mitochondrial redox signaling or insertion of copper into the active site of COX. Plays an essential role in embryo development.	FP [44] MS [6,9,37] TP: 1-13 [26]	N-Ace: 314 P-3	AT1G01910 [14]	[44,45]
HCC2	AT4G39740	Q8LAL0	Thioredoxin superfamily protein.	Encodes HCC2, resulting from a gene duplication during plant evolution. With sequence homology to Sco1 proteins, involved in copper insertion during COX assembly in other organisms. HCC2, which lacks the cysteines and histidine putatively involved in copper binding, functions in copper sensing and redox homeostasis.	FP [44] MS [9] TP: 1-14 [26]	NR	NR	[44–46]
COA6-L	AT5G58005	Q8RXH9		COX subunit VIb family protein.	MS [9]	UBI-21 [19]	NR	NR
COX11	AT1G02410	Q8GWR0	Cytochrome *c* oxidase assembly protein CtaG/Cox11 family.	Involved in the insertion of Cu_B into subunit COX1.	FP [47] MS [37] TP: 1-80 [26]	NR	AT4G09570 [34]	[47]
COX17-1	AT3G15352	Q9LJQ9	Cytochrome *c* oxidase 17.	Encodes a protein similar to yeast Cox17, a copper-binding protein that mediates the delivery of copper for COX assembly. Functionally complements the yeast *cox17* null mutant.	FP [48] MS [28]	Ace-28 [28] DIS 37-66, 47-56 [26] P-1 [49]	NR	[48,50–52]
COX17-2	AT1G53030	Q94FT1	Cytochrome *c* oxidase 17.	Encodes a protein similar to yeast Cox17, a copper-binding protein that mediates the delivery of copper for COX assembly. Functionally complements the yeast *cox17* null mutant.	MS [9]	DIS 35-64, 45-54 [26]	NR	[48,50–52]

COX19-1	AT1G66590	F4IEX1	Cytochrome *c* oxidase 19-1.	Cytochrome *c* oxidase 19-1. Functionally complements the yeast *cox19* null mutant.	Mitochondrion: 1.0 [21]	NR	NR	[53]
COX19-2	AT1G69750	Q9C9L6	Cytochrome *c* oxidase 19-2.	Cytochrome *c* oxidase 19-2. Functionally complements the yeast *cox19* null mutant.	MS [9]	NR	NR	[53]
COX23	AT1G02160	Q8VZ44	Cox19 family protein (CHCH motif).	Cox19 family protein (CHCH motif)	MS [9]	UBI-4 [19]	NR	NR
COX23L	AT5G09570	Q9LXC2	Cox19-like CHCH family protein.			NR	NR	NR
PET191	AT1G10865	Q8GWM1	Cytochrome *c* oxidase assembly factor.		Mitochondrion [26]	UBI-55 [19]	NR	NR
CMC1	AT5G16060	Q9LFR9	Cytochrome *c* oxidase assembly factor		MS [9]	Ace-23 [29]	AT1G22920 [14]	NR
CMC2	AT4G21192	Q0WSU0	Cytochrome *c* oxidase biogenesis protein; Cmc1-like protein		Mitochondrion [26]	UBI-4,64 [19]	NR	NR
PHT3-1	AT5G14040	Q9FMU6	Mitochondrial phosphate carrier protein.	Transport of phosphate from the cytosol to the mitochondrial matrix. Mediates salt stress tolerance through an ATP-dependent pathway and via modulation of gibberellin metabolism.	MS [4–10]	NR	AT5G43980 [54] AT3G51030 [55]	[10,39,56–58]
PHT3-2	AT3G48850	Q9M2Z8			FP [59] MS [4,6,9,28,37]	NR	NR	[39,57,58]
PHT3-3	AT2G17270	Q7DNC3			Mitochondrion: 0.91 [21]	NR	NR	NR
Mrs3-like	AT1G07030	Q8L6Z2	Mitochondrial substrate carrier family protein.	Integral component of the IMM; iron ion transmembrane transporter activity; iron ion homeostasis; mitochondrial iron ion transport.	MS [9,37]	N-Ace [29]	NR	NR
	AT2G30160	O64731			MS [9]	NR	NR	NR
	AT5G42130	Q9FHX2	MITOFERRIN-LIKE 1		MS [37]	NR	NR	[60]

Cox Assembly (Other)

	AGI	Swiss-Prot ID	Protein Name	Description	Experimental Evidence [a]	PTMS [b]	PPI [c]	Ref. [d]
COX assembly protein	AT4G14145	A0JPW4	Cytochrome c oxidase assembly protein.	Cytochrome c oxidase assembly protein.	MS [61]	NR	NR	NR
ATL48	AT3G48030	Q7X843	Hypoxia-responsive family protein.	Protein modification; protein ubiquitination.	MS [9]	P-1 [49] Ace [29]	NR	[62]
ATHIGD3	AT3g05550	Q9M9W0	Hypoxia-responsive family protein.		MS [35]	NR	NR	[35]
EMB2794	AT2G02150	P0C894	Putative pentatricopeptide repeat-containing protein	Tetratricopeptide repeat (TPR)-like superfamily protein.	Mitochondrion: 0.91 [21]	NR	NR	[63]
PPR superfamily protein	AT1G52640	Q9SSR6	Pentatricopeptide repeat (PPR) superfamily protein.		Mitochondrion: 0.91 [21,26]	P-1 [12]	NR	[63]
	AT5G16640	Q9FMD3	Pentatricopeptide repeat (PPR) superfamily protein		Mitochondrion: 0.91 [21,26]	NR	NR	NR
RFP2	AT1G62670	Q9SXD1	5′-mRNA PPR processing protein	Involved in the formation of COX3 mRNA 5′ ends.	Mitochondrion: 1.0 [21]	NR	AT4G26630 [64]	[63,64]
WTF9	AT2G39120	Q9ZUZ6	Ubiquitin carboxyl-terminal hydrolase family protein	Involved in the splicing of group II introns in mitochondria.	FP [65]	NR	NR	[66]
RIP1/MORF8	AT3G15000	Q9LKA5	Multiple organellar RNA editing factor.	Involved in organellar RNA editing. Required for the processing of numerous RNA editing sites in mitochondria and plastids.	FP [67,68] MS [6–10] Dual targeting to mitochondria and chloroplasts [67,68]	NR	AT3G27960 [14] AT5G10270 AT5G64960 [69] MEF10	[67,68,70]

							[71], PPOX1 [72], MORF1/RIP8; MORF2/RIP2; MORF3/RIP3; MORF4/RIP4; MORF5/RIP5; MORF6/RIP6 MORF7/RIP7, PMD1 [73], RBG3/ORRM3 RBG5/ORRM4 [74]ORRM1, VAT3/OZ1 [75] MEF35 [76], ORRM6 [77]	
MORF1	AT4G20020	O49429	Multiple organellar RNA editing factors.	Required for RNA editing in plant mitochondria and provides additional components of the RNA editing machinery in plant organelles.	FP [68] MS [7,9]	NR	MEF35 [76] MEF13 [78]	[79]
MEF21	AT2G20540	Q9SIL5	Pentatricopeptide repeat-containing protein.	Required for RNA editing in plant mitochondria.	Mitochondrion: 1.0 [21]	NR	AT4G20020 AT2G33430 AT1G11430 [78]	[63,80]
MEF26	AT3G03580	Q9SS60		Required for RNA editing in plant mitochondria.	Mitochondrion: 1.0 MitoProt2.	NR	NR	[81–83]
COD1	AT2G35030	O64766		PLS-subfamily PPR protein which is involved in the editing of two distant sites in the *COX2* transcript.	FP [21]	NR	NR	[84]
MEF13	AT3G02330	Q9FWA6		Involved in C-to-U editing of mitochondrial RNA. Required for RNA editing at 8 sites in 6 different mRNAs in mitochondria.	FP [21] MS [79]	NR	MORF1/RIP8, MORF8/RIP1 [79]	[79]
ORRM4	AT1G74230	Q9C909	Organelle RNA Recognition Motif-containing protein.	Functions as major mitochondrial editing factor. Controls 44% of the mitochondrial editing sites.	FP [74,85] MS [4,6,9,37,86]	NR	MORF8/RIP1 RBG3/ORRM3 [74]	[74,85,87]
mCSF-1	AT4G31010	Q8VYD9	CRS2-associated factor 1, mitochondrial.	CRM family member required for the processing of many mitochondrial introns. Involved in the biogenesis of respiratory complexes I and IV.	Mitochondrion: 1.0 [21]	NR	NR	[88]
NMAT2	AT5G46920	Q9FJR9	Nuclear intron maturase 2.	Nuclear-encoded maturase required for splicing of group-II introns in mitochondria. Associated to a large ribonucleoprotein complex in mitochondria containing group-II intron RNAs.	FP [89]	NR	NR	[89–91]
PMH2	AT3G22330	Q9LUW5	Putative mitochondrial RNA helicase 2.	Mitochondria-located protein required for efficient group II intron splicing in mitochondria.	FP [11] MS [4,6,9,10]	NR	NR	[11,92]
MIO24.13	AT5G51740	Q9FLI5	Peptidase family M48 family protein.	Peptidase family M48 family protein.	MS [4,6–10]	NR	NR	NR

Mitochondrial glycoprotein family	AT5G02050	Q9LZM6	Mitochondrial glycoprotein family protein.	Mitochondrial glycoprotein family protein.	MS [7,9]	NR	AT4G25200 [11]	NR
	AT1G80720	Q9SAI6			MS [9]	NR	NR	NR
	AT1G15870	Q9LMP8			Mitochondrion: 1.0 [21]	NR	NR	NR
	AT3G55605	Q8LCT2			MS [9,87]	NR	AT5G47590 [11]	NR
	AT5G05990	Q9FI87			MS [6,9]	P-1 [93]	NR	NR
	AT2G39795	Q8W487			MS [4,6,7,87] TP: 1-52 [26]	UBI-100 P-1 [94,95]	NR	[10,11]
	AT4G31930	Q9AST4			MS [9,37]	NR	NR	NR
	AT2G41600	Q3E7H1			MS [9]	UBI-7 [19]	NR	NR
mtHSC70-1	AT4G37910	Q8GUM2	Heat shock 70 kDa protein 9.	Stabilize preexistent proteins against aggregation and mediate the folding of newly translated polypeptides.	MS [11] TP: 1-46 [26]	NR P [12,95,96,]	AT5G09230 [97]	[98]
mtHSC70-2	AT5G09590	Q9LDZ0	Heat shock 70 kDa protein 10.		MS [11] TP: 1-50 [26]	P [95]	AT4G11260 [98]	[98,99]
MATR	ATMG00520	P93307	Maturase	Intron maturase, type II family protein.	Mitochondrion: 1.0 [21]	P-5 [100–102]	NR	NR

[a] Experimental evidence for mitochondrial localization and strategy of identification: FP (Fusion to Fluorescence Proteins), MS (Mass Spectrometry). [b] PTMS: Posttranslational protein modifications. The information was taken from the PLMD3.0 (http://plmd.biocuckoo.org/index.php, [96]) and PhosPhAT 4.0 (http://phosphat.uni-hohenheim.de/phosphat.html, [102]) databases. UBI: Ubiquitiation, Ace: Acetylation, P: Phosphorylation. [c] PPI: Reported evidences about Protein-Protein Interactions. Experimental information about PPI is from the UniProtKB database (http://www.uniprot.org/help/evidences, [26]). [d] Experimental evidence about the respective COX-related protein. NR: Not Reported; TP: presence of canonical Transit Peptide; DIS: Disulfide bridge.

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