

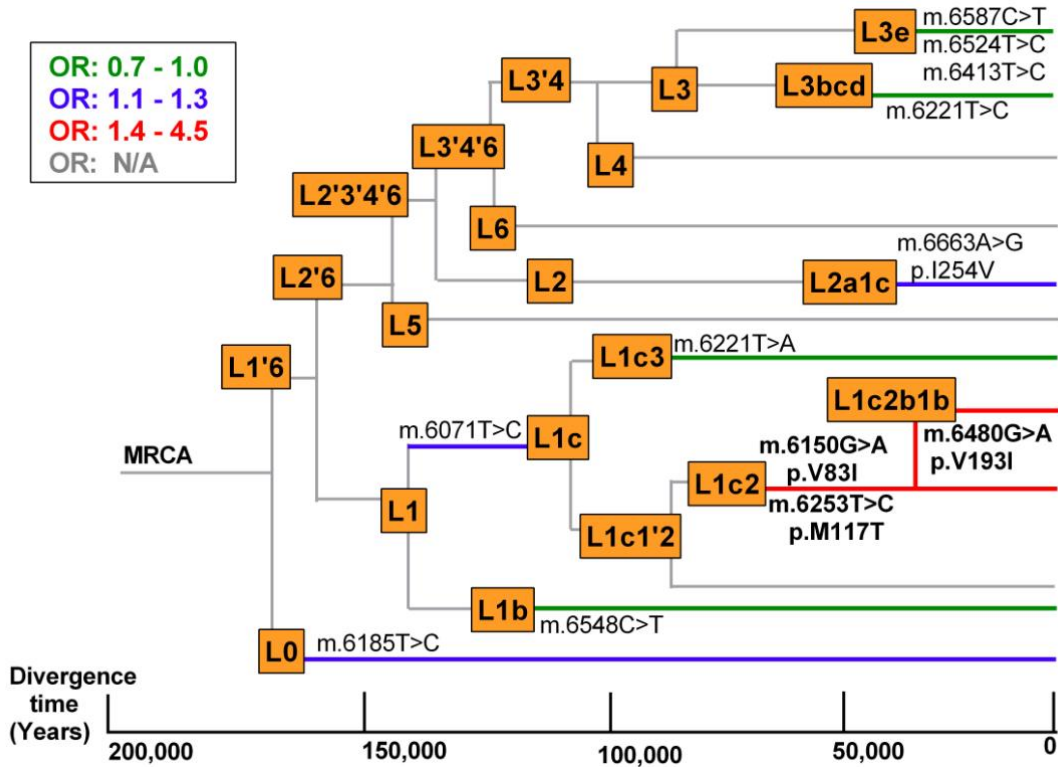
SUPPLEMENTARY ONLINE MATERIAL

Supplementary Table S1. Missense variants in CO1 identified by Sanger sequencing, AA POAG cases and controls (n=2,152 for position m.6150)*.

Variant (rCRS)	AA Change	SIFT prediction	SIFT score	Variant cases (obs.)	WT cases (obs.)	Variant controls (obs.)	WT controls (obs.)	p-value
m.5911C>T	A3V	neutral	0.11	11	895	2	379	0.37
m.5913G>A	D4N	neutral	0.47	5	903	0	386	0.33
m.5935A>G	N11S	neutral	0.05	0	968	1	477	0.33
m.5961C>A	L20M	deleterious	0.00	1	1023	0	550	1.00
m.5970G>A	G23S	neutral	0.08	2	1040	0	569	0.54
m.6039A>G	N46D	deleterious	0.04	0	1091	1	644	0.37
m.6040 A>C	N46T	deleterious	0.03	1	1090	1	644	1.00
m.6040A>G	N46S	neutral	0.42	2	1089	0	645	0.53
m.6052A>G	N50S	neutral	1.00	0	1168	1	742	0.39
m.6150G>A	V83I	neutral	0.20	72	1235	26	819	0.008
m.6249G>A	A116T	neutral	0.45	3	1305	2	844	1.00
m.6253T>C	M117T	neutral	0.09	60	1248	24	822	0.04
m.6267G>A	A122T	neutral	0.37	9	1299	7	839	0.80
m.6286T>C	V128A	neutral	0.22	3	1305	2	844	1.00
m.6339A>G	T146A	deleterious	0.00	1	1307	0	845	1.00
m.6340C>T	T146I	neutral	1.00	1	1307	1	844	1.00
m.6345T>C	F148L	deleterious	0.00	2	1306	1	844	1.00
m.6366G>A	V155I	neutral	0.11	4	1304	2	842	1.00
m.6367T>C	V155A	neutral	1.00	1	1307	0	844	1.00
m.6480G>A	V193I	neutral	0.23	14	1292	2	845	0.04
m.6481T>C	V193A	neutral	0.72	1	1304	1	846	1.00
m.6546C>T	L215F	deleterious	0.00	0	1300	1	846	0.39
m.6663A>G	I254V	neutral	0.69	40	1245	24	812	0.80
m.6678A>G**	T259A	neutral	0.25	1	1022	0	525	1.00

*. Lower sequencing coverage was obtained for positions other than m.6150. Table 1 in main text includes data on m.6150 from 37 subjects who subsequently enrolled in the study.

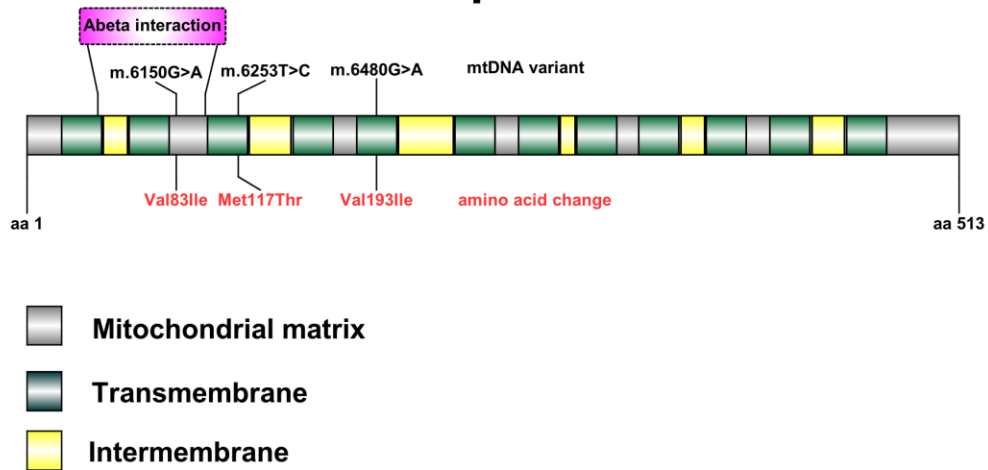
** = novel variant



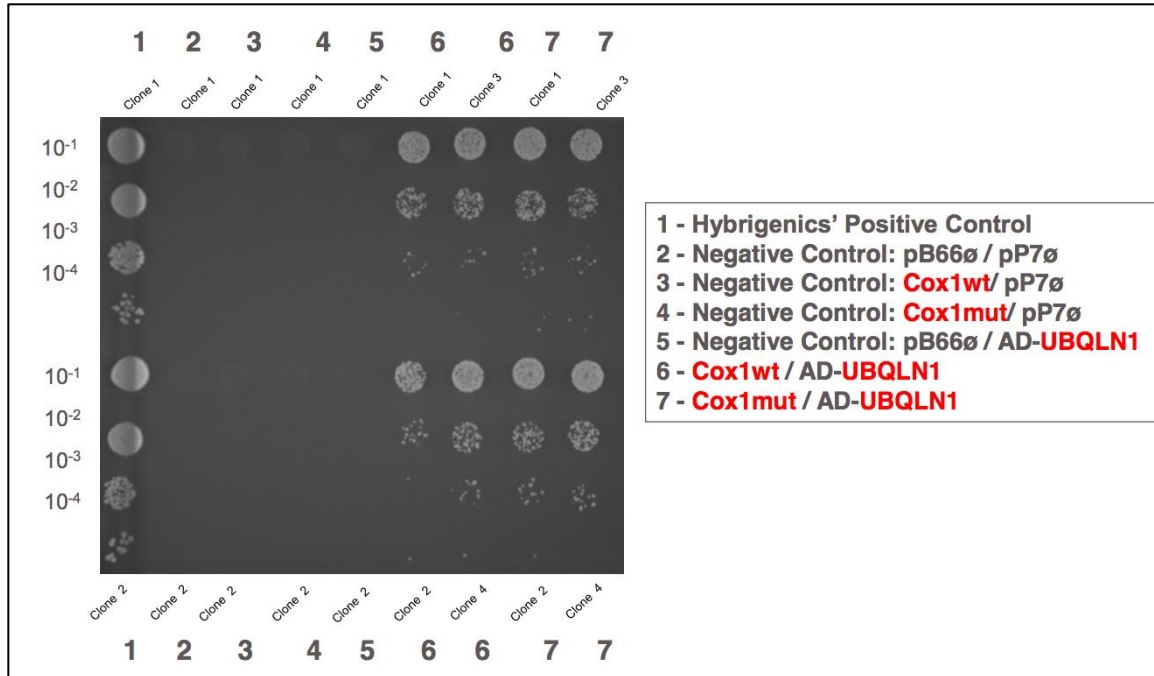
Supplementary Figure S1. Evolutionary relationship and POAG associations of common AA *MT-CO1* variants, from Sanger sequencing. Colored shading indicates the relative frequencies of the variants in cases : controls (odds ratio [OR]). Amino acid changes are indicated for missense variants, and the three missense variants with POAG association are highlighted with bold font. The m.6150G>A (V83I) variant was also observed on non-L1 lineages in POAAGG subjects (not shown).

MRCA=most recent common ancestor

Co1 protein



Supplementary Figure S2. Predicted domain structure of the CO1 protein and subcellular localizations of three POAG-associated missense variants.



Supplementary Figure S3. Quantification of interaction of wild type CO1 (“Cox1wt”) or V83I CO1 (“Cox1mut”) with UBQLN1 in the yeast two-hybrid system. The growth medium contained 10mM 3-AT, and cells were plated at four dilutions, as indicated at left.