Supplementary Material

Includes 3 tables and 1 figure.

Table S1. All germline variants in the HGSOC patients.

Position	Sequence changes	Locus	Amino acid change	Functional class	Status	GB Freq.	MitoTIP Score	Polyphen2 Score	Score Interpretation	Counts	Case#	Observed in cell or tissue type (MITOMAP)
73	A > G	MT-HV2			Homoplasmy	76466				16	soc1, soc5, soc7, soc10, soc11, soc12, soc14, soc15, soc16, soc17, soc18, soc19, soc20, soc21, soc23, soc24	aging brains, POLG/PEO & control muscle, buccal cell, thyroid & prostate tumors
114	C > T	MT-HV2/OHR			Homoplasmy	332				1	soc20	POLG/PEO muscle, bladder tumor back-mutation, BD-associated
146	T > C	MT-HV2/OHR			Homoplasmy	18543				2	soc15, soc23	ovarian carcinoma
150	C > T	MT-HV2/OHR			Homoplasmy	13908				4	soc1, soc7, soc19, soc20	elderly fibroblasts/leukocytes, lung, thyroid, prostate tumors
151	C > T	MT-HV2/OHR			Homoplasmy	3343				1	soc24	
152	T > C	MT-HV2/OHR			Homoplasmy	26471				6	soc7, soc12, soc14, soc17, soc18, soc24	elderly brains, elderly fibroblasts, ovarian carcinoma, breast tumor
183	A > G	MT-HV2/OHR			Homoplasmy	705				1	soc11	POLG/PEO muscle
195	T > C	MT-HV2/OHR			Homoplasmy	18627				2	soc20, soc14	elderly fibroblasts, elderly/AD brains, tumors: lung, thyroid, ovarian, prostate, glioblastoma, BD-associated / melanoma pts
207	G > A	MT-HV2/OHR			Homoplasmy	4269				2	soc15, soc17	oral, prostate & thyroid tumors
214	A > G	MT-HV2/OHR			Homoplasmy	426				2	soc10, soc18	
228	G > A	MT-HV2/OHR			Homoplasmy	1933				1	soc12	

235	A > G	MT-HV2/OHR/CSB1/TFX			Homoplasmy	3915				2	soc14, soc17	prostate tumor
248	delA	MT-HV2			Homoplasmy	6843				3	soc16, soc18, soc21	
263	A > G	MT-HV2/OHR			Homoplasmy	89941				15	soc1, soc5, soc7, soc10, soc11, soc12, soc14, soc15, soc16, soc18, soc19, soc20, soc21, soc23, soc24	POLG/MNGIE muscle
272	A > G	MT-HV2/OHR			Homoplasmy	81				1	soc24	
310C-tract	Multiple changes, includes np303-315	upstream			Homoplasmy:Heteroplasmy, 4:12	-				16	soc1, soc5, soc7, soc10, soc11, soc12, soc14, soc15, soc16, soc17, soc18, soc19, soc20, soc21, soc23, soc24	MSS
316	G > A	MT-HV2/OHR			Homoplasmy	1390				1	soc12	
368	A > G	MT-HV2/OHR			Homoplasmy	72				1	soc10	elderly fibroblasts
408	T > A	MT-OHR/LSP			Homoplasmy	187				1	soc15	elderly muscle, POLG/PEO, Twinkle/PEO frontal cortex and muscle, normal tissues
439	A > C	MT-OHR/LSP/TFL/HV3			Heteroplasmy, loss in ovarian cancer tissue	10				2	soc10, soc14	
456	C > T	MT-HV3			Homoplasmy	1936				1	soc7	thyroid tumor
471	T > C	MT-HV3			Homoplasmy	131				1	soc18	
489	T > C	MT-HV3			Homoplasmy	23766				6	soc5, soc7, soc18, soc19, soc21, soc24	ovarian carcinoma, prostate tumor
499	G > A	MT-HV3			Homoplasmy	3296				1	soc15	thyroid & prostate tumors
np514-523	Simple sequence repeats, delCA	upstream			Homoplasmy	-				5	soc5, soc11, soc 14, soc17, soc19	MSS
663	A > G	MT-RNR1			Homoplasmy	1404				2	soc14, soc17	Coronary Atherosclerosis risk
681	T > C	MT-RNR1			Homoplasmy	148				1	soc7	
709	G > A	MT-RNR1			Homoplasmy	6635				3	soc10, soc18, soc23	

750	A > G	MT-RNR1			Homoplasmy	50304				16	soc1, soc5, soc7, soc10, soc11, soc12, soc14, soc15, soc16, soc17, soc18, soc19, soc20, soc21, soc23, soc24	SZ-associated
752	C > T	MT-RNR1			Homoplasmy	216				1	soc19	
827	A > G	MT-RNR1			Homoplasmy	1291				2	soc12, soc15	DEAF
1005	T > C	MT-RNR1			Homoplasmy	230				1	soc16	DEAF
1048	C > T	MT-RNR1			Homoplasmy	1896				1	soc7	
1107	T > C	MT-RNR1			Homoplasmy	385				2	soc7, soc19	
1119	T > C	MT-RNR1			Homoplasmy	288				2	soc10, soc20	
1438	A > G	MT-RNR1			Homoplasmy	48542				15	soc1, soc5, soc7, soc10, soc11, soc12, soc14, soc15, soc16, soc17, soc18, soc20, soc21, soc23, soc24	DM/SZ-associated
1541	T > C	MT-RNR1			Homoplasmy	138				1	soc11	
1719	G > A	MT-RNR2			Homoplasmy	2435				1	soc17	
1736	A > G	MT-RNR2			Homoplasmy	1389				2	soc14, soc17	
1824	T > C	MT-RNR2			Homoplasmy	172				1	soc16	
2483	T > C	MT-RNR2			Homoplasmy	94				1	soc5	
2626	T > C	MT-RNR2			Homoplasmy	222				1	soc5	
2706	A > G	MT-RNR2			Homoplasmy	40409				3	soc14, soc19, soc20	
2772	C > T	MT-RNR2			Homoplasmy	175				1	soc5	
3010	G > A	MT-RNR2			Homoplasmy	7351				1	soc24	Cyclic Vomiting Syndrome with Migraine
3105	3106delC	MT-RNR2			Homoplasmy	2				16	soc1, soc5, soc7, soc10, soc11, soc12, sic14, soc15, soc16, soc17, soc18, soc19, soc20, soc21, soc23, soc24	
3206	C > T	MT-RNR2/RNR3			Homoplasmy	158				1	soc24	
3402	A > G	MT-ND1	p.Q32Q	synonymous SNV	Homoplasmy	5				1	soc19	
3497	C > T	MT-ND1	p.A64V	MISSENSE	Homoplasmy	185		0.009	benign	2	soc10, soc20	LHON

3552	T > A	MT-ND1	p.A82A	synonymous SNV	Homoplasmy	1779				1	soc21	
3756	A > G	MT-ND1	p.L150L	synonymous SNV	Homoplasmy	760				1	soc5	
3834	G > A	MT-ND1	p.L176L	synonymous SNV	Homoplasmy	448				1	soc23	
3918	G > A	MT-ND1	p.E204E	synonymous SNV	Homoplasmy	452				1	soc10	breast tumor
3970	C > T	MT-ND1	p.L222L	synonymous SNV	Homoplasmy	1898				2	soc11, soc16	
4227	A > G	MT-ND1	p.M307M	synonymous SNV	Homoplasmy	58				1	soc12	
4248	T > C	MT-ND1	p.I314I	synonymous SNV	Homoplasmy	1787				2	soc14, soc17	
4386	T > C	MT-TQ			Homoplasmy	168	3.0739		likely benign	2	soc1, soc5	Heart disease / myopathy / hypertension
4502	T > C	MT-ND2	p.S11S	synonymous SNV	Homoplasmy	69				1	soc18	
4715	A > G	MT-ND2	p.G82G	synonymous SNV	Homoplasmy	2218				2	soc18, soc21	
4769	A > G	MT-ND2	p.M100M	synonymous SNV	Homoplasmy	49949				16	soc1, soc5, soc7, soc10, soc11, soc12, soc14, soc15, soc16, soc17, soc18, soc19, soc20, soc21, soc23, soc24	SZ-associated
4820	G > A	MT-ND2	p.E117E	synonymous SNV	Homoplasmy	1219				1	soc15	
4824	A > G	MT-ND2	p.T119A	MISSENSE	Homoplasmy	1449		0.318	benign	2	soc14, soc17	
4853	G > A	MT-ND2	p.L128L	synonymous SNV	Homoplasmy	141				1	soc18	
4883	C > T	MT-ND2	p.P138P	synonymous SNV	Homoplasmy	2398				3	soc7, soc19, soc24	Glaucoma
4884	A > C	MT-ND2	p.I139L	MISSENSE	Homoplasmy	2		0.001	benign	1	soc11	
4924	G > A	MT-ND2	p.S152N	MISSENSE	Homoplasmy	69		0.003	benign	1		
4958	A > G	MT-ND2	p.M163M	synonymous SNV	Homoplasmy	140				1	soc5	
5048	T > C	MT-ND2	p.V193V	synonymous SNV	Heteroplasmy	158				1	soc5 (loss in ovarian cancer tissue)	

5147	G > A	MT-ND2	p.T226T	synonymous SNV	Homoplasmy	2208				1	soc12	
5153	A > G	MT-ND2	p.L228L	synonymous SNV	Homoplasmy	341				1	soc7	
5178	C > A	MT-ND2	p.L237M	MISSENSE	Homoplasmy	2375		0.92	probably damaging	3	soc7, soc19, soc24	Longevity; Extraversion MI / AMS protection; blood iron metabolism
5196	T > C	MT-ND2	p.L243L	synonymous SNV	Homoplasmy	101				1	soc20	
5231	G > A	MT-ND2	p.L254L	synonymous SNV	Homoplasmy	1169				1	soc1	endometrium control tissue，Normal in paired tumor tissue
5301	A > G	MT-ND2	p.I278V	MISSENSE	Homoplasmy	447		0.005	benign	2	soc7, soc19	
5417	G > A	MT-ND2	p.Q316Q	synonymous SNV	Homoplasmy	552				2	soc1, soc23	
5441	A > G	MT-ND2	p.P324P	synonymous SNV	Homoplasmy	29				1	soc20	
5466	A > G	MT-ND2	p.T333A	MISSENSE	Homoplasmy	24		0.009	benign	1	soc24	
5821	G > A	MT-TC			Homoplasmy	342	7.6717		likely benign	1	soc18	DEAF helper mut.
5895	delC	upstream			Homoplasmy	15				1	soc5	MSS
6023	G > A	MT-CO1	p.E40E	synonymous SNV	Homoplasmy	403				1	soc15	
6253	T > C	MT-CO1	p.M117T	MISSENSE	Homoplasmy	531		0	benign	1	soc7	Prostate Cancer / enriched in POAG cohort
6340	C > T	MT-CO1	p.T146I	MISSENSE	Homoplasmy	88		0.025	benign	1	soc14	Prostate Cancer
6392	T > C	MT-CO1	p.N163N	synonymous SNV	Homoplasmy	1853				1	soc16	
6413	T > C	MT-CO1	p.N170N	synonymous SNV	Homoplasmy	316				1	soc15	
6455	C > T	MT-CO1	p.F184F	synonymous SNV	Homoplasmy	1582				1	soc5	
6752	A > G	MT-CO1	p.L283L	synonymous SNV	Homoplasmy	341				1	soc18	
7028	C > T	MT-CO1	p.A375A	synonymous SNV	Homoplasmy	41344				16	soc1, soc5, soc7, soc10, soc11, soc12, soc14, soc15, soc16, soc17, soc18, soc19, soc20, soc21, soc23, soc24	
7196	C > A	MT-CO1	p.L431L	synonymous SNV	Homoplasmy	2072				2	soc18, soc21	

7220	T > C	MT-CO1	p.R439R	synonymous SNV	Homoplasmy	33				1	soc17	
7270	T > C	MT-CO1	p.V456A	MISSENSE	Homoplasmy	83		0.116	benign	1	soc7	
7828	A > G	MT-CO2	p.L81L	synonymous SNV	Homoplasmy	316				1	soc16	
7830	G > A	MT-CO2	p.R82H	MISSENSE	Homoplasmy	55		0.986	probably damaging	1	soc1	
8188	A > G	MT-CO2	p.G201G	synonymous SNV	Homoplasmy	342				1	soc21	
8270	8271_8279delACCCCCTCT	upstream			Homoplasmy	162				2	soc10, soc12	
8392	G > A	MT-ATP8	p.W9W	synonymous SNV	Homoplasmy	359				1	soc23	
8414	C > T	MT-ATP8	p.L17F	MISSENSE	Homoplasmy	1968		0.992	probably damaging	1	soc24	Longevity (protective factor)
8459	A > G	MT-ATP8	p.N32D	MISSENSE	Homoplasmy	113		0.974	probably damaging	1	soc17	
8473	T > C	MT-ATP8	p.P36P	synonymous SNV	Homoplasmy	538				2	soc15, soc24	
8584	G > A	MT-ATP6	p.A20T	MISSENSE	Homoplasmy	2834		0.012	benign	2	soc18, soc21	
8679	A > G	MT-ATP6	p.K51K	synonymous SNV	Homoplasmy	52				1	soc16	
8701	A > G	MT-ATP6	p.T59A	MISSENSE	Homoplasmy	17050		0.005	benign	6	soc5, soc7, soc18, soc19, soc21, soc24	thyroid tumors
8794	C > T	MT-ATP6	p.H90Y	MISSENSE	Homoplasmy	1399		0.003	benign	2	soc14, soc17	Exercise Endurance / Coronary Atherosclerosis risk
8860	A > G	MT-ATP6	p.T112A	MISSENSE	Homoplasmy	50409		0.003	benign	16	soc1, soc5, soc7, soc10, soc11, soc12, soc14, soc15, soc16, soc17, soc18, soc19, soc20, soc21, soc23, soc24	
9055	G > A	MT-ATP6	p.A177T	MISSENSE	Homoplasmy	2178		0.399	benign	1	soc15	PD (protective factor)
9077	T > C	MT-ATP6	p.I184T	MISSENSE	Homoplasmy	74		0.003	benign	1	soc21	
9090	T > C	MT-ATP6	p.S188S	synonymous SNV	Homoplasmy	206				1	soc18	
9180	A > G	MT-ATP6	p.V218V	synonymous SNV	Homoplasmy	477				2	soc7, soc19	
9182	G > A	MT-ATP6	p.S219N	MISSENSE	Homoplasmy	48		0.978	probably damaging	1	soc5	
9233	T > C	MT-CO3	p.H9H	synonymous SNV	Homoplasmy	68				1	soc5	

9338	A > T	MT-CO3	p.M44I	MISSENSE	Homoplasmy	26		0.001	benign	1	soc15	
9540	T > C	MT-CO3	p.L112L	synonymous SNV	Homoplasmy	17044				6	soc5, soc7, soc18, soc19, soc21, soc24	tumor
9545	A > G	MT-CO3	p.G113G	synonymous SNV	Homoplasmy	2417				1	soc21	
9615	T > C	MT-CO3	p.L137L	synonymous SNV	Homoplasmy	96				1	soc15	
9716	T > A	MT-CO3	p.G170G	synonymous SNV	Homoplasmy	6				1	soc14	
9824	T > C	MT-CO3	p.L206L	synonymous SNV	Homoplasmy	1464				1	soc5	
10208	T > C	MT-ND3	p.P50P	synonymous SNV	Homoplasmy	83				1	soc18	
10310	G > A	MT-ND3	p.L84L	synonymous SNV	Homoplasmy	1844				2	soc10, soc16	
10379	A > G	MT-ND3	p.L107L	synonymous SNV	Homoplasmy	5				1	soc23	
10397	A > G	MT-ND3	p.W113W	synonymous SNV	Homoplasmy	427				2	soc7, soc19	
10398	A > G	MT-ND3	p.T114A	MISSENSE	Homoplasmy	22565		0	benign	8	soc5, soc7, soc18, soc19, soc20, soc21, soc23, soc24	PD protective factor / longevity / altered cell pH / metabolic syndrome / breast cancer risk
10400	C > T	MT-ND3	p.T114T	synonymous SNV	Homoplasmy	10840				6	soc5, soc7, soc18, soc19, soc21, soc24	
10535	T > C	MT-ND4L	p.Y22Y	synonymous SNV	Homoplasmy	188				1	soc16	
10586	G > A	MT-ND4L	p.S39S	synonymous SNV	Homoplasmy	870				1	soc16	
10736	C > T	MT-ND4L	p.Y89Y	synonymous SNV	Homoplasmy	28				1	soc11	
10757	C > G	MT-ND4L	p.L96L	synonymous SNV	Homoplasmy	2				1	soc12	
10790	T > C	MT-ND4	p.L11L	synonymous SNV	Homoplasmy	140				1	soc10	
10810	T > C	MT-ND4	p.L17L	synonymous SNV	Homoplasmy	2688				1	soc16	
10873	T > C	MT-ND4	p.P38P	synonymous SNV	Homoplasmy	17033				6	soc5, soc7, soc18, soc19, soc21, soc24	

11017	T > C	MT-ND4	p.S86S	synonymous SNV	Homoplasmy	136				1	soc5	
11077	A > G	MT-ND4	p.L106L	synonymous SNV	Homoplasmy	7				1	soc11	
11084	A > G	MT-ND4	p.T109A	MISSENSE	Homoplasmy	204		0.988	probably damaging	2	soc5, soc17	AD, PD; MELAS
11152	T > C	MT-ND4	p.A131A	synonymous SNV	Homoplasmy	120				1	soc19	pancreatic cancer cell line
11377	G > A	MT-ND4	p.K206K	synonymous SNV	Homoplasmy	644				1	soc10	
11428	C > A	MT-ND4	p.A223A	synonymous SNV	Homoplasmy	3				1	soc12	
11719	G > A	MT-ND4	p.G320G	synonymous SNV	Homoplasmy	39624				16	soc1, soc5, soc7, soc10, soc11, soc12, soc14, soc15, soc16, soc17, soc18, soc19, soc20, soc21, soc23, soc24	
11809	T > C	MT-ND4	p.T350T	synonymous SNV	Homoplasmy	75				1	soc14	
11914	G > A	MT-ND4	p.T385T	synonymous SNV	Homoplasmy	5754				2	soc12, soc21	
11944	T > C	MT-ND4	p.L395L	synonymous SNV	Homoplasmy	1606				1	soc19	
11974	A > G	MT-ND4	p.L405L	synonymous SNV	Homoplasmy	61				1	soc17	pancreatic cancer cell line
12007	G > A	MT-ND4	p.W416W	synonymous SNV	Homoplasmy	3313				1	soc1	
12026	A > G	MT-ND4	p.I423V	MISSENSE	Homoplasmy	246		0.01	benign	1	soc19	DM
12172	A > G	MT-TH			Homoplasmy	343	3.3266		likely benign	1	soc11	
12192	G > A	MT-TH			Homoplasmy	112	2.6593		likely benign	1	soc19	MICM
12248	A > G	MT-TS2			Homoplasmy	105	3.692		likely benign	1	soc10	
12338	T > C	MT-ND5	p.M1T	MISSENSE	Homoplasmy	174		Unknown	Unknown	1	soc16	DEAF1555 increased penetrance / LHON
12358	A > G	MT-ND5	p.T8A	MISSENSE	Homoplasmy	775		Unknown	Unknown	1	soc1	
12361	A > G	MT-ND5	p.T9A	MISSENSE	Homoplasmy	277		Unknown	Unknown	1	soc10	Nonalcoholic fatty liver disease
12372	G > A	MT-ND5	p.L12L	synonymous SNV	Homoplasmy	6929				1	soc1	prostate tumor，Altered brain pH / sCJD patients
12406	G > A	MT-ND5	p.V24I	MISSENSE	Homoplasmy	1380		0.001	benign	1	soc10	

12634	A > G	MT-ND5	p.I100V	MISSENSE	Homoplasmy	147		0.943	probably damaging	1	soc19	Thyroid Cancer Cell Line
12705	C > T	MT-ND5	p.I123I	synonymous SNV	Homoplasmy	21208				10	soc1, soc5, soc7, soc14, soc17, soc18, soc19, soc21, soc23, soc24	prostate tumor
12714	T > C	MT-ND5	p.I126I	synonymous SNV	Homoplasmy	177				1	soc11	
12732	T > C	MT-ND5	p.V132V	synonymous SNV	Homoplasmy	98				1	soc12	
12771	G > A	MT-ND5	p.E145E	synonymous SNV	Homoplasmy	571				1	soc5	
12904	A > G	MT-ND5	p.I190V	MISSENSE	Heteroplasmy	53		0.01	benign	1	soc16 (loss in ovarian cancer tissue)	
12981	C > T	MT-ND5	p.G215G	synonymous SNV	Homoplasmy	4				1	soc15	
13263	A > G	MT-ND5	p.Q309Q	synonymous SNV	Homoplasmy	1866				1	soc21	
13590	G > A	MT-ND5	p.L418L	synonymous SNV	Homoplasmy	2885				1	soc15	
13629	A > G	MT-ND5	p.L431L	synonymous SNV	Homoplasmy	18				1	soc20	
13650	C > T	MT-ND5	p.P438P	synonymous SNV	Homoplasmy	3970				1	soc14	
13708	G > A	MT-ND5	p.A458T	MISSENSE	Homoplasmy	3666		0.001	benign	1	soc16	acute leukemia platelets, leukocytes & bone marrow, breast tumor；LHON / Increased MS risk / higher freq in PD-ADS，Heteroplasmic in acute leukemia, homoplasmic or absent in earlier stage.
13788	C > T	MT-ND5	p.L484L	synonymous SNV	Homoplasmy	15				1	soc17	
13810	G > A	MT-ND5	p.A492T	MISSENSE	Homoplasmy	47		0.017	benign	1	soc18	
13928	G > C	MT-ND5	p.S531T	MISSENSE	Homoplasmy	2467		0.18	benign	2	soc11, soc16	
13942	A > G	MT-ND5	p.T536A	MISSENSE	Homoplasmy	45		0.074	benign	1	soc12	

14067	C > T	MT-ND5	p.T577T	synonymous SNV	Homoplasmy	69				1	soc17	
14100	C > T	MT-ND5	p.F588F	synonymous SNV	Homoplasmy	14				1	soc16	
14133	A > G	MT-ND5	p.L599L	synonymous SNV	Homoplasmy	469				1	soc15	
14178	T > C	MT-ND6	p.I166V	MISSENSE	Homoplasmy	1092		0.023	benign	1	soc23	
14305	G > A	MT-ND6	p.S123S	synonymous SNV	Homoplasmy	353				1	soc18	
14318	T > C	MT-ND6	p.N119S	MISSENSE	Homoplasmy	1790		0.017	benign	1	soc21	
14364	G > A	MT-ND6	p.L104L	synonymous SNV	Homoplasmy	413				1	soc5	
14392	C > T	MT-ND6	p.V94V	synonymous SNV	Homoplasmy	11				1	soc20	
14560	G > A	MT-ND6	p.V38V	synonymous SNV	Homoplasmy	1145				1	soc16	
14668	C > T	MT-ND6	p.M2M	synonymous SNV	Homoplasmy	2065				1	soc24	Depressive Disorder associated
14693	A > G	MT-TE			Homoplasmy	265	11.4662		possibly benign	1	soc23	MELAS / LHON / DEAF / hypertension helper
14766	C > T	MT-CYB	p.T7I	MISSENSE	Homoplasmy	39357		0	benign	16	soc1, soc5, soc7, soc10, soc11, soc12, soc14, soc15, soc16, soc17, soc18, soc19, soc20, soc21, soc23, soc24	
14783	T > C	MT-CYB	p.L13L	synonymous SNV	Homoplasmy	10816				6	soc5, soc7, soc18, soc19, soc21, soc24	
14979	T > C	MT-CYB	p.I78T	MISSENSE	Homoplasmy	171		0.067	benign	1	soc24	
15038	A > G	MT-CYB	p.I98V	MISSENSE	Homoplasmy	27		0.807	possibly damaging	1	soc12	
15043	G > A	MT-CYB	p.G99G	synonymous SNV	Homoplasmy	12019				6	soc5, soc7, soc18, soc19, soc21, soc24	MDD-associated
15080	A > G	MT-CYB	p.T112A	MISSENSE	Homoplasmy	70		0.994	probably damaging	1	soc21	
15172	G > A	MT-CYB	p.G142G	synonymous SNV	Homoplasmy	394				1	soc24	endometrial tumor
15191	T > C	MT-CYB	p.L149L	synonymous SNV	Homoplasmy	75				1	soc5	

15301	G > A	MT-CYB	p.L185L	synonymous SNV	Homoplasmy	14598				6	soc5, soc7, soc18, soc19, soc21, soc24	tumor
15326	A > G	MT-CYB	p.T194A	MISSENSE	Homoplasmy	50503		0.009	benign	16	soc1, soc5, soc7, soc10, soc11, soc12, soc14, soc15, soc16, soc17, soc18, soc19, soc20, soc21, soc23, soc24	
15346	G > A	MT-CYB	p.L200L	synonymous SNV	Homoplasmy	406				2	soc10, soc20	
15412	T > C	MT-CYB	p.P222P	synonymous SNV	Homoplasmy	83				1	soc24	
15479	T > C	MT-CYB	p.F245L	MISSENSE	Homoplasmy	193		0.012	benign	1	soc19	
15487	A > T	MT-CYB	p.P247P	synonymous SNV	Homoplasmy	2084				2	soc18, soc21	
15535	C > T	MT-CYB	p.N263N	synonymous SNV	Homoplasmy	1179				2	soc12, soc15	
15724	A > G	MT-CYB	p.W326W	synonymous SNV	Homoplasmy	132				1	soc7	
15784	T > C	MT-CYB	p.P346P	synonymous SNV	Homoplasmy	1770				1	soc18	POAG - potential for association
15930	G > A	MT-TT			Homoplasmy	1246	2.3888		likely benign	1	soc12	
15941	T > C	MT-TT			Homoplasmy	877	2.8613		likely benign	1	soc20	
16086	T > C	MT-HV1/TAS2			Homoplasmy	2752				2	soc15, soc17	
16092	T > C	MT-HV1/TAS2			Homoplasmy	2234				2	soc7, soc12	
16111	C > T	MT-HV1/TAS2			Homoplasmy	3978				1	soc1	colonic crypts, prostate tumor
16126	T > C	MT-HV1/TAS2			Homoplasmy	12581				1	soc23	glioblastoma, normal tissues
16129	G > A	MT-HV1/TAS2			Homoplasmy	18313				2	soc1, soc24	Cyclic Vomiting Syndrome with Migraine
16136	T > C	MT-HV1/TAS2			Homoplasmy	1320				1	soc15	
16145	G > A	MT-HV1			Homoplasmy	3866				1	soc11	
16164	A > G	MT-HV1/TAS			Homoplasmy	621				1	soc19	

16171	A > T	MT-HV1/TAS			Homoplasmy	21				1	soc19	
16172	T > C	MT-HV1/TAS			Homoplasmy	10296				1	soc19	MNGIE tissues, head/neck tumor back-mutation
16182	A > C	MT-HV1			Heteroplasmy	8492				4	soc10, soc15, soc19, soc20	prostate tumor
16183	A > C	MT-HV1			Heteroplasmy	18155				5	soc10, soc12, soc15, soc19, soc20	lung tumor back-mutation, prostate tumor，Melanoma patients
16185	C > T	MT-HV1			Homoplasmy	1574				1	soc18	
16189	T > C	MT-HV1			Homoplasmy	32494				5	soc10, soc12, soc15, soc19, soc20	prostate tumor,normal buccal swab，Diabetes / Cardiomyopathy / Endometrial cancer risk / mtDNA copy nbr / Metabolic Syndrome / Melanoma patients
16192	C > T	MT-HV1			Homoplasmy	5359				1	soc11	Melanoma patients
16203	A > G	MT-HV1/MT-5			Homoplasmy	294				1	soc16	
16209	T > C	MT-HV1			Homoplasmy	3136				1	soc5	
16217	T > C	MT-HV1			Homoplasmy	8548				4	soc10, soc12, soc15, soc20	prostate tumor
16223	C > T	MT-HV1			Homoplasmy	57418				9	soc1, soc5, soc7, soc14, soc17, soc18, soc19, soc21, soc24	tumor
16231	T > C	MT-HV1			Homoplasmy	1040				1	soc23	
16243	T > C	MT-HV1			Homoplasmy	2585				1	soc11	
16249	T > C	MT-HV1			Homoplasmy	2899				1	soc24	prostate tumor
16257	C > A	MT-HV1			Homoplasmy	976				1	soc1	
16260	C > T	MT-HV1			Homoplasmy	2056				1	soc18	gastric carcinoma
16261	C > T	MT-HV1			Homoplasmy	8342				1	soc1	
16265	A > G	MT-HV1			Homoplasmy	933				1	soc17	
16266	C > T	MT-HV1			Homoplasmy	2439				2	soc19, soc23	
16274	G > A	MT-HV1			Homoplasmy	3769				1	soc7	prostate tumor
16278	C > T	MT-HV1			Homoplasmy	12296				1	soc18	ovarian control tissue

16288	T > C	MT-HV1			Homoplasmy	1062				1	soc21	
16290	C > T	MT-HV1			Homoplasmy	6575				2	soc14, soc17	breast tumor
16298	T > C	MT-HV1			Homoplasmy	8340				1	soc21	prostate tumor
16304	T > C	MT-HV1			Homoplasmy	11502				2	soc11, soc16	esophageal, breast & prostate tumors
16311	T > C	MT-HV1			Homoplasmy	23464				1	soc14	
16319	G > A	MT-HV1			Homoplasmy	8966				3	soc14, soc17, soc23	
16324	T > C	MT-HV1			Homoplasmy	1010				1	soc5	esophageal cancer
16327	C > T	MT-HV1			Homoplasmy	5230				1	soc21	
16357	T > C	MT-HV1			Homoplasmy	1596				1	soc10	hair
16362	T > C	MT-HV1			Homoplasmy	28316				6	soc5, soc7, soc14, soc17, soc19, soc24	
16390	G > A	upstream			Homoplasmy	7464				2	soc11, soc21	breast, ovarian tumor, POAG - potential for association
16399	A > G	upstream			Homoplasmy	3097				1	soc23	gastric carcinoma
16519	T > C	upstream			Homoplasmy	62812				8	soc7, soc11, soc12, soc14, soc15, soc16, soc21, soc23	glioblastoma, gastric, lung, ovarian, prostate tumors, Cyclic Vomiting Syndrome with Migraine /metastasis

Note: the reference sequence is rCRS.

The GB fre. (GenBank frequency) data is obtained from MITOMAP database and is derived from 51192 GenBank sequences with size greater than 15.4kbp and 74326 Control Region sequences with size 0.4-1.6kbp (Updated (27 Jul 2020).

Table S2. The 27 somatic mtDNA mutations in the study patients.

Case #	Position	Base change	Heteroplasmy	Locus	Amino acid change	Functional class	Regions	GB Freq.	MitoTIP	Polyphen2	Score Interpretation	Observed in cell or tissue type (MITOMAP)
SOC1	439	A > C	0.28	MT-OHR/LSP/TFL/HV3			d-loop	10				
SOC12	439	A > C	0.23	MT-OHR/LSP/TFL/HV4			d-loop	10				
SOC15	439	A > C	0.26	MT-OHR/LSP/TFL/HV5			d-loop	10				
SOC16	439	A > C	0.25	MT-OHR/LSP/TFL/HV			d-loop	10				
SOC23	439	A > C	0.23	MT-OHR/LSP/TFL/HV7			d-loop	10				
SOC7	1045	G > A	0.56	MT-RNR1			rRNA	Novel				
SOC1	1273	G > A	0.08	MT-RNR1			rRNA	Novel				
SOC5	1360	G > A	0.65	MT-RNR1			rRNA	Novel				
SOC20	1592	T > C	0.80	MT-RNR1			rRNA	Novel				
SOC11	2876	G > A	0.16	MT-RNR2			rRNA	Novel				
SOC5	3173	G > A	0.11	MT-RNR2			rRNA	13				
SOC5	3566	3566insC	0.34	MT-ND1	p.T87fs	frameshift insertion	protein coding region	Novel			damaging	colorectal tumor, oncocytoma
SOC1	4175	G > A	0.42	MT-ND1	p.W290X	stop-gain SNV	protein coding region	Novel			damaging	
SOC12	4813	T > C	0.08	MT-ND2	p.V115A	missense	protein coding region	2		0.535	possibly damaging	
SOC7	5269	T > C	0.58	MT-ND2	p.I267T	missense	protein coding region	Novel		0.808	possibly damaging	
SOC10	5540	G > A	0.16	MT-TW			tRNA	Novel	16.1127		possibly pathogenic	encephalomyopathy / DEAF
SOC23	6382	G > A	0.73	MT-CO1	p.G160E	missense	protein coding region	Novel		0.925	probably damaging	
SOC21	6579	G > A	0.27	MT-CO1	p.G226X	stop-gain SNV	protein coding region	Novel			damaging	
SOC15	8383	T > C	0.23	MT-ATP8	p.T6T	synonymous SNV	protein coding region	155				
SOC16	9478	9478delT	0.41	MT-CO3	p.V91fs	frameshift deletion	protein coding region	Novel			damaging	MSI
SOC18	11152	T > C	0.42	MT-ND4	p.A131A	synonymous SNV	protein coding region	120				pancreatic cancer cell line
SOC17	11902	G > A	0.09	MT-ND4	p.V381V	synonymous SNV	protein coding region	39				
SOC17	12814	G > A	0.82	MT-ND5	p.A160T	missense	protein coding region	1		0.998	probably damaging	
SOC14	13201	G > A	0.2	MT-ND5	p.A289T	missense	protein coding region	Novel		0.999	probably damaging	
SOC24	14968	T > C	0.15	MT-CYB	p.N74N	synonymous SNV	protein coding region	30				
SOC14	14979	T > C	0.21	MT-CYB	p.I78T	missense	protein coding region	171		0.067	benign	
SOC12	16182	A > C	0.13	MT-HV1			d-loop	8492				
SOC7	16183	A > C	0.11	MT-HV1			d-loop	18155				lung tumor back-mutation, prostate tumor, melanoma patients

Note: The GB fre. (GenBank frequency) data is obtained from MITOMAP database and is derived from 51192 GenBank sequences with size greater than 15.4kbp and 74326 Control Region sequences with size 0.4-1.6kbp (Updated 27 Jul 2020).
Disease-associated information of the detected mtDNA variants were retrieved form MITOMAP (Updated 27 Jul 2020).

Table S3. Summary statement of DNA base change characteristics in all sequence variants of this study.

	Germline variants, 569 variants Number (%)							Somatic mutations, 28 mutations Number (%)					
	Total	d-loop	rRNA	tRNA	interge nic	protein coding region non-sys‡	syn	Total	d-loop	rRNA	tRNA	protein coding region non-syn‡	syn
Transversions													
A:T→C:G	12 (2.1)	11 (1.9)	-	-	-	1 (0.2)	-	7 (25.0)	7 (25.0)	-	-	-	-
A:T→T:A	7 (1.2)	2 (0.4)	-	-	-	1 (0.2)	4 (0.7)	-	-	-	-	-	-
G:C→T:A	7 (1.2)	1 (0.2)	-	-	-	3 (0.5)	3 (0.5)	-	-	-	-	-	-
G:C→C:G	3 (0.5)	-	-	-	-	2 (0.4)	1 (0.2)	-	-	-	-	-	-
Transitions													
A:T→G:C	311 (54.7)	100 (17.6)	50 (8.8)	6 (1.1)	-	70 (12.3)	85 (14.9)	7 (25.0)	-	1 (3.6)	-	3 (10.7)	3 (10.7)
G:C→A:T	186 (32.7)	41 (7.2)	9 (1.6)	3 (0.5)	-	31 (5.4)	102 (17.9)	12 (42.9)	-	5 (17.9)	1 (3.6)	5 (17.9)	1 (3.6)
Small indels	43 (7.6)	24 (4.2)	16 (2.8)	-	3 (0.5)	-	-	2 (7.1)				2 (7.1)	-

Note: non-sys‡ includes nonsynonymous variants, and missense and truncating mutations; -, not observed

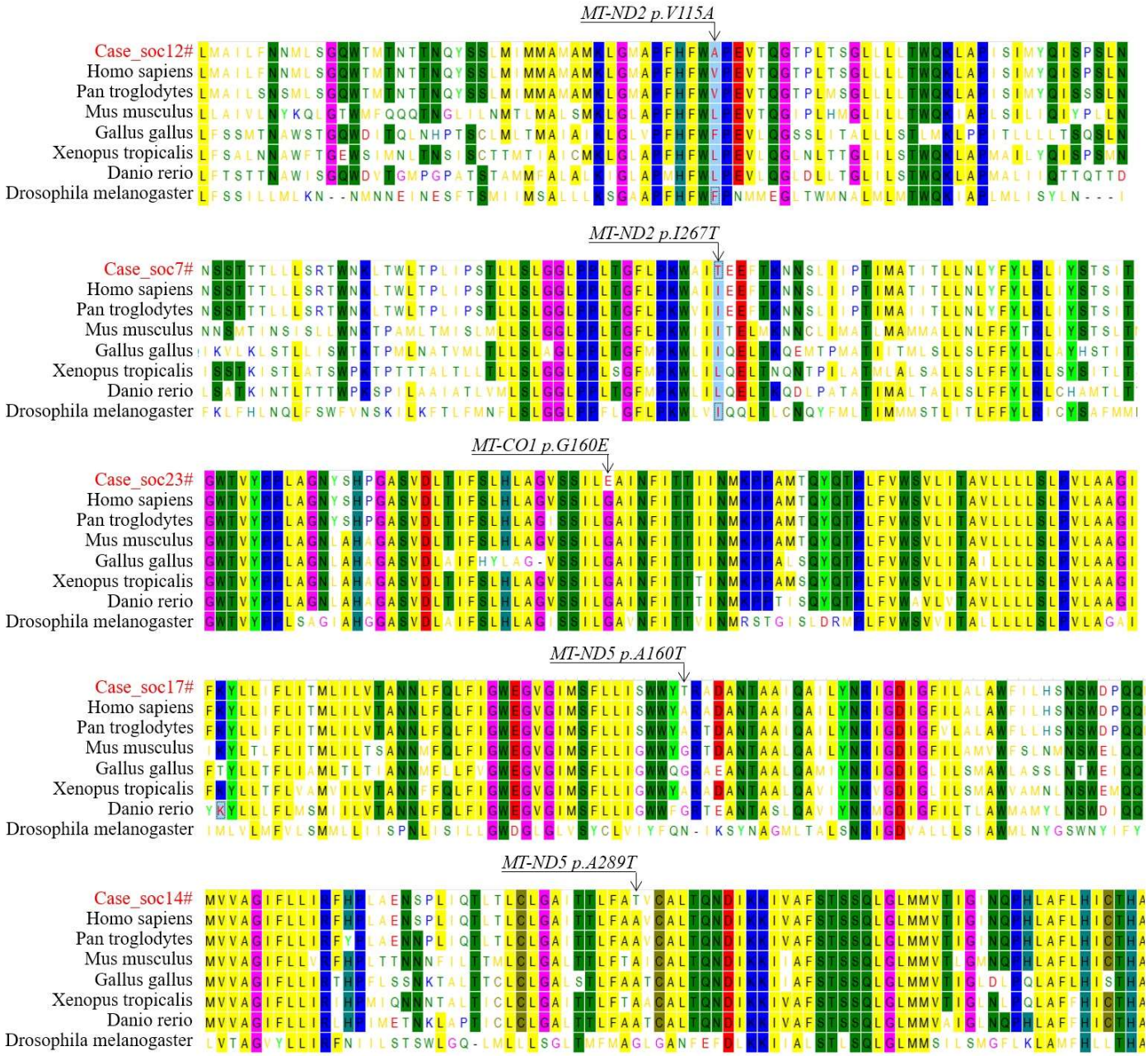

Figure S1. Homogeneous analysis of amino acids sequences for the identified tumor-specific missense mutations.