

**Title:** Association of predicted pathogenic mutations in mitochondrial *ND* genes with distant metastasis in NSCLC and colon cancer

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Supplementary Table S1. Nonsynonymous SNPs and SNVs in the *ND* genes in NSCLC and colon cancer clinical samples.

NSCLC primary tissue (45 cases)				None	Conserved amino acid substitution	Novel mutation								
ID	Age/Sex	Histology	TNM*1	ND1	ND2	ND3	ND4L	ND4	ND5	ND6	COII	ATP6	CYTB	
LgCa-150	71/M	Squamous cell carcinoma	T3N2M0		G4705A (M79T) A4824G (T119A)				T12880C (F182L)			A8563G (T13A) C8794T (H90Y)	C14766T (T7I) A15326G (T194A)	
LgCa-151	57/M	Squamous cell carcinoma	T2N0M0			A10398G (T114A)		G11696A (V313I)				A8701G (T59A)	C14766T (T7I) A15326G (T194A)	
LgCa-152	59/F	Adenocarcinoma	T4N0M0			A10398G (T114A)						A8701G (T59A)	C14766T (T7I) T14979C (I78T) A15326G (T194A)	
LgCa-153	64/M	Large cell carcinoma	T4N2M1 (Mediastinal LN meta)			A10398G (T114A)		A11084G (T109A)			G8075A (A164T)	A8531G (N2S) A8701G (T59A)	C14766T (T7I) A15326G (T194A)	
LgCa-154	76/F	Squamous cell carcinoma	T1N0M0			A10398G (T114A)						A8701G (T59A) T8762C (I79T)	C14766T (T7I) A15326G (T194A)	
LgCa-157	63/M	Squamous cell carcinoma	T1N0M0			A10398G (T114A)						A8701G (T59A)	C14766T (T7I) A15326G (T194A)	
LgCa-159	59/M	Squamous cell carcinoma	T2N1M0		A4833G (T122A)	A10398G (T114A)			G12622A (V96I)			A8701G (T59A)	C14766T (T7I) A15326G (T194A)	
LgCa-161	71/M	Adenocarcinoma	T2N1M0			A10398G (T114A)		A11084G (T109A)				A8701G (T59A)	C14766T (T7I) A15326G (T194A)	
LgCa-162	62/M	Large cell carcinoma	T1N0M0	G4048A (D248N)	G5460A(A331T)	T10345C (I96T) T10398G (T114A)			T12811C (Y159H)		G7653A (V90I)	A8701G (T59A)	C14766T (T7I) A15326G (T194A)	
LgCa-163	57/M	Adenocarcinoma	T1N0M0			A10398G (T114A)			G13708A (A458T)			A8701G (T59A)	C14766T (T7I) A15326G (T194A)	
LgCa-164	37/M	Adenocarcinoma	T1N0M0			A10398G (T114A)		A11084G (T109A)				A8701G (T59A)	C14766T (T7I) A15326G (T194A)	
LgCa-165	79/F	Adenocarcinoma	T2N2M0			A10398G (T114A)						A8701G (T59A)	C14766T (T7I) T14979C (I78T) A15326G (T194A)	
LgCa-166	71/M	Squamous cell carcinoma	T4N2M0						A12358G (T8A)				C14766T (T7I) A15326G (T194A)	
LgCa-167	56/F	Adenocarcinoma	T1N0M0						A12358G (T8A)				C14766T (T7I) A15326G (T194A)	
LgCa-168	61/F	Adenocarcinoma	T1N0M0			A10398G (T114A)			G13477A (A381T)	T14502C (I58V)		A8701G (T59A)	C14766T (T7I) A14870G (I42V) T15071C (Y109H) A15218G (T158A) A15326G (T194A)	
LgCa-169	72/M	Squamous cell carcinoma	T1N1M0	G3391A (G29S) G3709A (A135T) (heteroplasmy or mixture)		A10398G (T114A)						A8701G (T59A)	C14766T (T7I) A15326G (T194A)	
LgCa-173	74/M	Squamous cell carcinoma	T3N0M0		T5344C (F292S) (heteroplasmy or mixture) G5460A (A331T)	T10345C (I96T) T10398G (T114A)			T12811C (Y159H) G13103A (G256E) (heteroplasmy or mixture)		A case with two selected mutations	G7853A (V90I)	A8701G (T59A)	C14766T (T7I) G14804A (D20N) A15326G (T194A)
LgCa-174	59/M	Adenocarcinoma	T2N1M0		G4704A (M79L) A4824G (T119A)							A8563G (T13A) C8794T (H90Y)	C14766T (T7I) A15326G (T194A)	
LgCa-175	46/F	Adenocarcinoma	T1N0M0									T9101G (I192S) (homoplasmy)	C14766T (T7I) A15326G (T194A)	
LgCa-176	80/M	Squamous cell carcinoma	T1N0M0		T4705C (M79T) A4732G (N88S)		T10609C (M47T)		G12406A (V24I) G13928C (S531T)				C14766T (T7I) A15326G (T194A)	
LgCa-177	43/F	Squamous cell carcinoma	T1N0M0			A10398G (T114A)						A8701G (T59A)	C14766T (T7I) A15326G (T194A)	
LgCa-178	58/M	Squamous cell carcinoma	T1N1M0	T4216C (Y304H)	A5301G (I278V)	A10398G (T114A)			A13105G (I257V)			A8701G (T59A)	C14766T (T7I) A14927G (T61A) A15326G (T194A)	

LgCa-179	54/F	Adenocarcinoma	T1N0M0			A10398G (T114A)				
LgCa-180	68/M	Adenocarcinoma	T2N1M0		A4824G (T119A)				T12880C (F182L)	
LgCa-181	64/M	Squamous cell carcinoma	T1N2M0			A10398G (T114A)				
LgCa-182	46/M	Adenocarcinoma	T1N2M0			A10398G (T114A)		A11084G (T109A)		
IgCa-183	67/M	Squamous cell carcinoma	T2N0M0							
LgCa-184	52/M	Pleomorphic carcinoma	T3N0M0						A12358G (T8A)	
LgCa-187	73/M	Adenocarcinoma	T1N0M0		T4705C (M79T) A4732G (N88S)		T10609C (M47T)		G12406A (V24I) G13928C (S531T)	
LgCa-188	59/M	Squamous cell carcinoma	T1N0M0			A10398G (T114A)				
LgCa-189	73/M	Squamous cell carcinoma	T1N1M0		A5301G (I278V)	A10398G (T114A)			A13651C (T439P)	T14319C (N119D)
LgCa-190	62/M	Adenocarcinoma	T2N1M0					G11016A (S86N)	A13183G (I283V)	
LgCa-191	50/M	Adenocarcinoma	T2N2M0			A10398G (T114A)			A12361G (T9A)	
LgCa-192	54/F	Adenocarcinoma	T4N0M0		G4705A (M79T) A4824G (T119A)					
LgCa-193	76/M	Squamous cell carcinoma	T1N0M0			A10398G (T114A)				
LgCa-194	41/M	Adenocarcinoma	T2N2M0		A5301G (I278V)	A10398G (T114A)				
LgCa-195	66/M	Bronchioalveolar carcinoma	T1N0M0							
LgCa-196	64/M	Adenocarcinoma	T1N0M0	C3497T (A64V)	A4704C (M79L)					
LgCa-197	59/M	Bronchioalveolar carcinoma	T1N0M0	T3394C (Y30H)	G4491A (V8I)	G10290A (A78T) (heteroplasmy or mixture) A10389G (T114T)		G11963A (V402I)		
LgCa-198	35/M	Squamous cell carcinoma	T?N1M0			A10398G (T114A)		A11084G (T109A)		
LgCa-199	63/M	Adenocarcinoma	T1N1M0						A12358G (T8A)	
LgCa-200	58/F	Adenocarcinoma	T1N0M0	G4048A (D248N)	G5460A (A331T)	T10345C (I96T) T10389G (T114T)			T12811C (Y159H)	
LgCa-201	64/M	Adenocarcinoma	T1N0M0			A10398G (T114A)			A12361G (T9A)	
LgCa-202	76/M	Adenocarcinoma	T1N0M0			A10398G (T114A)				
LgCa-205	74/F	Squamous cell carcinoma	T1N1M0			A10398G (T114A)		G11696A (V313I)		

\*1 TNM (Tumour/Node/Metastasis) classification for staging of cancer.

**NSCLC metastases (37 cases)**

ID	Age/Sex	Histology	Metastatic site	None						Conserved amino acid substitution	Novel mutation
				ND1	ND2	ND3	ND4L	ND4	ND5	ND6	
LuAdBrM-1	-	Adenocarcinoma	Brain			A10398G (T114A)			A11084G (T109A)	C12813A (Y159STOP) (heteroplasmy or mixture)	

		C14766T (T7I) A15326G (T194A)
	A8563G (T13A) C8794T (H90Y)	C14766T (T7I) A15326G (T194A)
	G8584A (A20T) A8701G (T59A)	C14766T (T7I) A15326G (T194A)
	T8602C (F26L) A8701G (T59A)	C14766T (T7I) A15326G (T194A)
		C14766T (T7I) T14798C (F18L) A15236G (I164V) A15326G (T194A)
		C14766T (T7I) A15326G (T194A)
	A8701G (T59A)	C14766T (T7I) T14979C (I78T) A15326G (T194A)
	A8701G (T59A)	C14766T (T7I) A15326G (T194A)
		C14766T (T7I) A15326G (T194A)
	G8584A (A20T)	C14766T (T7I) A15326G (T194A)
	A8563G (T13A) C8794T (H90Y)	C14766T (T7I) A15326G (T194A)
	A8701G (T59A)	C14766T (T7I) A15326G (T194A)
	A8701G (T59A)	C14766T (T7I) A15326G (T194A)
		C14766T (T7I) A15326G (T194A)
	A8701G (T59A)	C14766T (T7I) A15326G (T194A)
		C14766T (T7I) A15326G (T194A)
G7853A (V90I)	A8701G (T59A)	C14766T (T7I) A15326G (T194A)
	G8584A (A20T)	C14766T (T7I) G14985A (R80H) A15326G (T194A)
	A8701G (T59A)	C14766T (T7I) A15326G (T194A)
	A8701G (T59A)	C14766T (T7I) A15326G (T194A)

COI1	ATP6	CYT6
	A8701G (T59A)	C14766T (T7I) A15326G (T194A)

LuAdBrM-2	64/M	Adenocarcinoma	Brain	C3497T (A64V)							
LuAdBrM-3	-	Adenocarcinoma	Brain			A10398G (T114A)		A11084G (T109A)			
LuAdBrM-4	-	Adenocarcinoma	Brain		A4824G (T119A)	T10363C (L102P) (heteroplasmy or mixture)					
LuAdBrM-5	79/M	Adenocarcinoma	Brain	T3394C (Y30H) [T3394C (Y30H)]	G4491A (V8I)	A10398G (T114A)		G11963A (V402I)			
LuAdBrM-6	-	Adenocarcinoma	Brain	C3689G (A128G) (heteroplasmy or mixture)		T10084C (I9T)			A12358G (T8A)		
LuAdBrM-7	49/M	Adenocarcinoma	Brain		T4612C (M48T) A5127G (N220D)			G11969A (A404T) C11151T (A131V)	A13105G (I257V)		
LuAdBrM-8	70/M	Adenocarcinoma	Brain	T3394C (Y30H) [T3394C (Y30H)]	G4491A (V8I)	A10398G (T114A)		G11963A (V402I)			
LuAdBrM-9	-	Adenocarcinoma	Brain	C3497T (A64V)				A11930G (I391V) (homoplasmy)	A12361G (T9A)		
LuAdBrM-10	51/M	Adenocarcinoma	Brain		C5178A (L237M)	A10398G (T114A)			A14053G (T573A)		
LuAdBrM-11	-	Adenocarcinoma	Brain			A10398G (T114A)			G13135A (A267T)	T14502C (I58V) C14347T (V113M) (homoplasmy)	
LuAdBrM-12	-	Adenocarcinoma	Brain			A10398G (T114A)					
LuAdBrM-13	46/M	Adenocarcinoma	Brain	T3394C (Y30H) [T3394C (Y30H)]		A10398G (T114A)					
LuAdBrM-14	-	Adenocarcinoma	Brain						A12358G (T8A)		
LuAdBrM-15	50/M	Adenocarcinoma	Brain			A10398G (T114A)		A11084G (T109A)	T13768C (F478L)		
LuAdBrM-16	69/M	Adenocarcinoma	Brain		C5178A (L237M)	A10398G (T114A)					
LuAdBrM-17	50/F	Adenocarcinoma	Brain			A10398G (T114A)			A12361G (T9A)		
LuAdBrM-18	-	Adenocarcinoma	Brain		A4824G (T119A)			C11409T (P217L) (heteroplasmy or mixture)		A14193G (F161L)	
LuAdBrM-19	47/M	Adenocarcinoma	Brain			A10398G (T114A)			A12361G (T9A)		
LuAdBrM-20	70/M	Adenocarcinoma	Brain	G4048A (D248N)	G5460A (A331T)	T10345C (I96T) A10389G (T114A)			T12811C (Y159H)		
LuAdBrM-22	72/M	Adenocarcinoma	Brain		C5178A (L237M)	A10398G (T114A)					
LuAdBrM-23	-	Adenocarcinoma	Brain		C5178A (L237M)	A10398G (T114A)					
LuAdBrM-24	68/F	Adenocarcinoma	Brain			A10398G (T114A)		A11084G (T109A)			
LuAdBrM-25	74/F	Adenocarcinoma	Brain		G4705A (M79T) A4732G (N88S)		T10609C (M47T)	G12406A (V24I) G13928C (S531T)			
LuPoBrM-1	-	Adenocarcinoma	Brain	C3497T (A64V)	A4704C (M79L)						
LuPoBrM-2	-	Adenoarcinoma	Brain	C3497T (A64V)					T13879C (S515P)	G14162A (A171V)	
LuPoBrM-3	-	Adenoarcinoma	Brain		A4824G (T119A) T5361C (Y298H) (heteroplasmy or mixture)						

											C14766T (T7I) A15326G (T194A)
		A8701G (T59A)									C14766T (T7I) A15326G (T194A)
		A8563G (T13A) C8794T (H90Y)									C14766T (T7I) A15326G (T194A)
		A8701G (T59A)									C14766T (T7I) A15326G (T194A)
											C14766T (T7I) A15326G (T194A)
		A8701G (T59A)									C14766T (T7I) A15326G (T194A)
											C14766T (T7I) A15326G (T194A)
		A8701G (T59A)									C14766T (T7I) A15326G (T194A)
											C14766T (T7I) A15326G (T194A)
		A8701G (T59A)									C14766T (T7I) A15326G (T194A)
											C14766T (T7I) A15326G (T194A)
		A8701G (T59A)									C14766T (T7I) A15326G (T194A)
											C14766T (T7I) A15326G (T194A)
		G8584A (A20T)									C14766T (T7I) A15326G (T194A)
											C14766T (T7I) A15326G (T194A)
		A8701G (T59A)									C14766T (T7I) A15326G (T194A)
											C14766T (T7I) A15326G (T194A)
		G8584A (A20T)									C14766T (T7I) A15326G (T194A)
		A8563G (T13A) C8794T (H90Y)									C14766T (T7I) A15326G (T194A)
		G8584A (A20T) A8894T (N123I)									C14766T (T7I) A14750G (T2A) A15326G (T194A)
	G7853A (V90I)	A8701G (T59A)									C14766T (T7I) A15326G (T194A)
		A8701G (T59A)									C14766T (T7I) A15326G (T194A)
		A8701G (T59A) T8762C (I79T)									C14766T (T7I) A15326G (T194A)
		A8701G (T59A)									C14766T (T7I) A15326G (T194A)
											C14766T (T7I) A15326G (T194A)
											C14766T (T7I) A15326G (T194A)
											C14766T (T7I) A15326G (T194A)
		C8794T (H90Y)									C14766T (T7I) A15326G (T194A)





Supplementary Table S2. Nonsynonymous SNPs and SNVs in the *ND* genes observed in NSCLC and colon cancer clinical samples.

Novel mutation

SNP/Mutation	Amino acid substitution	Homoplasmy or heteroplasmy	Frequency T (this study) (%)	Frequency C (mtSNP-Japan)*1 (%)	Frequency (T/C)*2	Grantham value	Evolutionary conservation of the original amino acid	Conformational change	Reported disease association*3	MutPred score*4	No. of cases detected			
											NSCLC		Colon Cancer	
											Primary (N=45)	Metastases (N=37)	Primary (N=22)	Metastases (N=11)
<b>ND1</b>														
G3391A	G29S	Homoplasmy	1/115 (0.87%)	10/672 (1.49%)	0.58	56			LHON (putative)	0.862	1	0	0	0
T3394C	Y30H	Homoplasmy	5/115 (4.35%)	14/672 (2.08%)	2.09	83	Conserved		LHON / Diabetes / CPT deficiency / high altitude adaptation	0.783	1	3	1 w/ liver meta	0
T3398C	M31T	Homoplasmy	1/115 (0.87%)	2/672 (0.30%)	2.9	81	Conserved		DMDF+HCM / GDM / possibly LVNC cardiomyopathy-associated	0.751	0	0	1	0
C3497T	A64V	Homoplasmy	7/115 (6.09%)	20/672 (2.98%)	2.04	64		Yes	LHON	0.413	1	5	0	1
C3689G	A128G	Heteroplasmy or Heterogeneous	2/115 (1.74%)	0	-	60		Yes		0.747	0	1	0	1
G3709A	A135T	Heteroplasmy or Heterogeneous	1/115 (0.87%)	0	-	58	Conserved	Yes		0.774	1	0	0	0
G3736A	V144I	Homoplasmy	2/115 (1.74%)	1/672 (0.15%)	11.6	29	Conserved		LHON	0.661	0	0	1 w/ liver meta (matched case 1)	1 (matched case 1)
G3955A	A217T	Heteroplasmy or Heterogeneous	1/115 (0.87%)	0	-	58		Yes		0.736	0	0	0	1
G4048A	D248N	Homoplasmy	4/115 (3.48%)	32/672 (4.76%)	0.73	23				0.37	2	1	1	0
T4067C	L254P	Heteroplasmy or Heterogeneous	1/115 (0.87%)	0	-	98				0.804	0	0	1	0
T4216C	Y304H	Homoplasmy	1/115 (0.87%)	2/672 (0.30%)	2.9	83	(Haplogroup JT)		LHON / Insulin Resistance /possible adaptive high altitude variant	0.611	1	0	0	0
<b>ND2</b>														
G4491A	V8I	Homoplasmy	3/115 (2.61%)	11/672 (1.64%)	1.59	29				0.439	1	2	0	0
T4612C	M48T	Homoplasmy	1/115 (0.87%)	3/672 (0.45%)	2.22	81				0.602	0	1	0	0
A4704C	M79L	Homoplasmy	3/115 (2.61%)	1/672 (0.15%)	17.4	15				0.686	2	1	0	0
T4705C	M79T	Homoplasmy	9/115 (7.83%)	9/672 (1.34%)	5.98	81				0.7	4	2	2 (1 w/ liver meta)	1
A4732G	N88S	Homoplasmy	6/115 (5.22%)	19/672 (2.83%)	1.84	46				0.292	2	1	2	1
A4824G	T119A	Homoplasmy	9/115 (7.83%)	50/672 (7.44%)	1.05	58	(Haplogroup A)			0.368	4	3	2	0
A4833G	T122A	Homoplasmy	3/115 (2.61%)	58/672 (8.63%)	0.3	58	(Haplogroup G)		Diabetes helper mutation/AD/PD	0.488	1	0	1	1
A5127G	N220D	Homoplasmy	1/115 (0.87%)	3/672 (0.45%)	1.93	23				0.528	0	1	0	0

C5178A	L237M	Homoplasmy	7/115 (6.09%)	261/673 (38.84%)	0.16	15	(Haplogroup D)		Longevity/Extraversion MI /AMS protection/ blood iron metabolism	0.26	0	5	0	2
A5301G	I278V	Homoplasmy	6/115 (5.22%)	29/672 (4.32%)	1.21	29				0.311	3	1	2	0
T5344C	F292S	Heteroplasmy or Heterogeneous	1/115 (0.87%)	0	-	22	Conserved			0.59	1	0	0	0
T5361C	Y298H	Heteroplasmy or Heterogeneous	1/115 (0.87%)	0	-	83	Conserved			0.685	0	1	0	0
T5418C	F317L	Homoplasmy	2/115 (1.74%)	0	-	22				0.612	0	0	1 w/ liver meta	1
T5442C	F325L	Homoplasmy	2/115 (1.74%)	4/672 (0.60%)	2.9	22				0.437	0	1	1	0
G5460A	A331T	Homoplasmy	5/115 (4.35%)	38/672 (5.65%)	0.77	58			PD/AD (controversial)	0.505	3	1	1	0
ND3														
T10084C	I9T	Homoplasmy	2/115 (1.74%)	11/672 (1.64%)	1.06	89				0.414	0	1	0	1
G10290A	A78T	Heteroplasmy or Heterogeneous	1/115 (0.87%)	0	-	58				0.669	1	0	0	0
T10345C	I96T	Homoplasmy	5/115 (4.35%)	29/672 (4.32%)	1	89				0.398	3	1	1	0
T10363C	L102P	Heteroplasmy or Heterogeneous	1/115 (0.87%)	0	-	98	Conserved			0.746	0	1	0	0
A10398G	T114A	Homoplasmy	67/115 (58.26%)	478/672 (71.13%)	0.82	58	(Haplogroup IJK)		PD protective factor / longevity / altered cell pH / metabolic syndrome / breast cancer risk	0.17	28	20	13	7
ND4L														
T10609C	M47T	Homoplasmy	8/115 (6.96%)	35/672 (5.21%)	1.34	81				0.481	2	2	2 (1 w/ liver meta)	2
ND4														
G11016A	S86N	Homoplasmy	2/115 (1.74%)	19/672 (2.83%)	0.62	46				0.303	1	0	0	1
A11084G	T109A	Homoplasmy	12/115 (10.43%)	38/672 (5.65%)	1.85	58			AD/PD/MELAS (controversial)	0.482	5 (1 w/ mediastinal LN meta)	4	2 w/ liver meta	1
C11151T	A131V	Homoplasmy	1/115 (0.90%)	5/672 (0.74%)	1.22	64				0.577	0	1	0	0
C11409T	P217L	Heteroplasmy or Heterogeneous	1/115 (0.90%)	0	-	98	Conserved			0.83	0	1	0	0
A11510G	N251D	Heteroplasmy or Heterogeneous	1/115 (0.90%)	0	-	23				0.364	0	0	1	0
G11696A	V313I	Homoplasmy	3/115 (2.61%)	5/672 (0.74%)	3.53	29			LHON / LDYT / DEAF / hypertension helper mutation	0.581	2	0	1	0
A11930G	I391V	Homoplasmy	2/115 (1.74%)	0	-	29				0.553	0	2	0	0
G11963A	V402I	Homoplasmy	3/115 (2.61%)	7/672 (1.04%)	2.51	29				0.369	1	2	0	0
G11969A	A404T	Homoplasmy	1/115 (0.90%)	4/672 (0.60%)	1.5	58				0.639	0	1	0	0



A12026G	I423V	Homoplasmy	1/115 (0.90%)	17/672 (2.53%)	0.36	29			DM	0.277	0	0	1	0
C12135T	S459F	Homoplasmy	2/115 (1.74%)	1/672 (0.15%)	11.6	155				0.319	0	0	1 w/ liver meta (matched case 2)	1 (matched case 2)
ND5														
T12338C	M1T	Homoplasmy	1/115 (0.90%)	2/672 (0.30%)	3	81	Conserved		DEAF1555 increased penetrance / LHON	0.966	0	0	1	0
A12358G	T8A	Homoplasmy	7/115 (6.09%)	40/672 (5.95%)	0.88	58				0.265	4	2	0	1
A12361G	T9A	Homoplasmy	5/115 (4.35%)	25/672 (3.72%)	1.02	58				0.249	2	3	0	0
G12406A	V24I	Homoplasmy	9/115 (7.83%)	39/672 (5.80%)	1.35	29				0.251	2	3	2	2
G12454 A	V40I	Homoplasmy	1/115 (0.90%)	0	-	29				0.528	0	0	1 w/ liver meta	0
G12503A	C56Y	Heteroplasmy or Heterogeneous	1/115 (0.90%)	0	-	194				0.399	0	0	1	0
G12622A	V96I	Homoplasmy	1/115 (0.90%)	1/672 (0.15%)	6	29				0.403	1	0	0	0
T12811C	Y159H	Homoplasmy	5/115 (4.35%)	29/672 (4.32%)	1.01	83			Possible LHON factor	0.587	3	1	1	0
C12813A	Y159STOP	Heteroplasmy or Heterogeneous	1/115 (0.90%)	0	-	-	Truncated			-	0	1	0	0
T12880C	F182L	Homoplasmy	2/115 (1.74%)	22/672 (3.27%)	0.53	22				0.635	2	0	0	0
G13103A	G256E	Heteroplasmy or Heterogeneous	1/115 (0.90%)	0	-	98	Conserved			0.834	1	0	0	0
A13105G	I257V	Homoplasmy	2/115 (1.74%)	7/672 (1.04%)	1.67	29				0.35	1	1	0	0
G13135A	A267T	Homoplasmy	1/115 (0.90%)	7/672 (1.04%)	0.87	58				0.452	0	1	0	0
A13183G	I283V	Homoplasmy	1/115 (0.90%)	18/672 (2.68%)	0.34	29				0.48	1	0	0	1
G13366A	G344STOP	Heteroplasmy or Heterogeneous	1/115 (0.90%)	0	-	-	Truncated			-	0	0	1	0
G13477A	A381T	Homoplasmy	1/115 (0.90%)	2/672 (0.30%)	3	58				0.601	1	0	0	0
A13651C	T439P	Homoplasmy	1/115 (0.90%)	11/672 (1.64%)	0.55	38				-	1	1	0	0
G13708A	A458T	Homoplasmy	2/115 (1.74%)	19/672 (2.83%)	0.78	58	(Haplogroup J)		LHON / Increased MS risk / higher freq in PD-ADS	0.409	1	0	1	0
G13759A	A475T	Homoplasmy	1/115 (0.90%)	15/672 (2.23%)	0.4	58				0.556	0	0	0	1
T13768C	F478L	Homoplasmy	1/115 (0.90%)	3/672 (0.45%)	2	22				0.572	0	1	0	0
T13879C	S515P	Homoplasmy	1/115 (0.90%)	5/672 (0.74%)	1.22	74				0.426	0	1	0	1
G13928C	S531T	Homoplasmy	10/115 (8.70%)	2/672 (0.30%)	29	58	(Haplogroup F)			0.321	2	3	3	2
A13942G	T536A	Homoplasmy	2/115 (1.74%)	2/672 (0.30%)	5.8	58				0.438	0	0	1	1
C14003T	T556I	Homoplasmy	1/115 (0.90%)	1/672 (0.15%)	6	89				0.533	0	0	1	0

A14053G	T573A	Homoplasmy	1/115 (0.90%)	4/672 (0.60%)	1.5	58				0.409	0	1	0	0
A14062G	I576V	Homoplasmy	1/115 (0.90%)	0	-	29				0.421	0	0	1	0
T14138C	L601P	Heteroplasmy or Heterogeneous	1/115 (0.90%)	0	-	98	Conserved			0.762	0	0	0	1
<b>ND6</b>														
G14162A	A171V	Homoplasmy	2/115 (1.74%)	4/672 (0.60%)	2.9	64				0.597	0	1	0	1
A14193G	F161L	Homoplasmy	1/115 (0.87%)	0	-	22				0.653	0	1	0	0
T14318C	N119S	Homoplasmy	1/115 (0.87%)	2/672 (0.30%)	2.9	46				0.437	0	1	0	0
T14319C	N119D	Homoplasmy	1/115 (0.87%)	0	-	23			PD, early onset	0.446	1	0	0	0
C14347T	V113M	Homoplasmy	1/115 (0.87%)	0	-	21				-	0	1	0	0
T14502C	I58V	Homoplasmy	2/115 (1.74%)	5/672 (0.74%)	2.35	29	Conserved		LHON	0.385	1	1	0	0
14504delA	L57STOP	Homoplasmy	1/115 (0.87%)	0	-	-		Truncated		-	0	0	1	0

**Novel mutation**

SNP/Mutation	Amino acid substitution	Homoplasmy or heteroplasmy	Frequency T (this study) (%)	Frequency C (mtSNP-Japan)*1 (%)	Frequency (T/C)*2	Grantham value	Evolutionary conservation of the original amino acid	Conformational change	Reported disease association*3	MutPred score*4	No. of cases detected			
											NSCLC		Colon Ca	
											Primary (N=45)	Metastases (N=37)	Primary (N=22)	Metastases (N=11)
<b>COII</b>														
G7598A	A5T	Homoplasmy	1/115 (0.87%)	1/672 (0.15%)	5.8	58			Possible LHON helper variant	0.342	0	1	0	0
G7616A	D11N	Homoplasmy	1/115 (0.87%)	0	-	23	Conserved			0.532	0	0	1	0
G7664A	A27T	Homoplasmy	2/115 (1.74%)	6/672 (0.89%)	1.96	58				0.518	0	1	0	1
G7853A	V90I	Homoplasmy	2/115 (1.74%)	30/672 (4.46%)	0.39	29				0.249	2	1	0	0
G7859A	D92N	Homoplasmy	1/115 (0.87%)	2/672 (0.30%)	2.9	23			Progressive Encephalomyopathy	0.226	0	1	1	0
G8075A	A164T	Homoplasmy	1/115 (0.87%)	1/672 (0.15%)	5.8	58				0.74	1	0	0	0
T8223C	L213S	Heteroplasmy or Heterogeneous	1/115 (0.87%)	0	-	145				0.478	0	0	0	1
<b>ATP6</b>														
A8531G	N2S	Homoplasmy	1/115 (0.87%)	0	-	46				0.651	1	0	0	0
A8563G	T13A	Homoplasmy	5/115 (4.35%)	44/672 (6.55%)	0.66	53				0.405	2	2	1 w/ liver meta	0
G8584A	A20T	Homoplasmy	5/115 (4.35%)	50/672 (7.44%)	0.58	58				0.553	1	4	0	0
T8602C	F26L	Homoplasmy	1/115 (0.87%)	0	-	22				0.614	1	0	0	0
A8701G	T59A	Homoplasmy	56/114 (49.12%)	425/672 (63.24%)	0.78	58				0.14	29	15	11	6
T8762C	I79T	Homoplasmy	2/115 (0.87%)	2/672 (0.30%)	2.9	89				0.687	1	1	0	0

C8794T	H90Y	Homoplasmy	7/115 (6.09%)	48/672 (7.14%)	0.85	83			Exercise Endurance / Coronary Atherosclerosis risk	0.608	1	3	2 (1 w/ liver meta)	0
A8894T	N123I	Homoplasmy	1/115 (0.87%)	4/672 (0.60%)	1.45	149				0.417	0	1	0	0
G9053A	S176N	Homoplasmy	1/115 (0.87%)	16/672 (2.38%)	0.37	46				0.37	0	0	0	1
C9099A	I191M	Homoplasmy	1/115 (0.87%)	1/672 (0.15%)	5.8	10				0.601	0	1	0	0
T9101G	I192S	Homoplasmy	1/115 (0.87%)	0	-	142			LHOH	0.529	1	0	0	0
<b>CYTB</b>														
A14750G	T2A	Homoplasmy	1/115 (0.87%)	4/672 (0.6%)	1.45	58				0.157	1	0	0	0
C14766T	T7I	Homoplasmy	115/115 (100%)	672/672 (100%)	1	89				0.165	45	37	22	11
T14798C	F18L	Homoplasmy	1/115 (0.87%)	0	-	22				0.609	1	0	0	0
G14804A	D20N	Homoplasmy	1/115 (0.87%)	0	-	23				0.716	1	0	0	0
A14870G	I42V	Homoplasmy	1/115 (0.87%)	1/672 (0.15%)	5.8	29				0.326	1	0	0	0
T14934C	F63S	Homoplasmy	1/115 (0.87%)	0	-	155				0.725	0	0	1 w/ liver meta	0
T14979C	I78T	Homoplasmy	5/115 (4.35%)	42/672 (6.25%)	0.7	89				0.239	3	2	1	1
G14985A	R80H	Homoplasmy	1/115 (0.87%)	0	-	29				0.833	1	0	0	0
T15071C	Y109H	Homoplasmy	2/115 (1.74%)	4/672 (0.6%)	2.9	83				0.554	1	1	0	
A15218G	T158A	Homoplasmy	2/115 (1.74%)	10/672 (1.49%)	1.17	58				0.366	1	0	1 w/ liver meta	0
A15236G	I164V	Homoplasmy	3/115 (2.61%)	16/672 (2.38%)	1.1	29				0.224	1	1	0	1
G15254A	V170M	Heteroplasmy or Heterogeneous	2/115 (1.74%)	0	-	21				0.719	0	0	1 w/ liver meta	1
G15314A	A190T	Homoplasmy	1/115 (0.87%)	6/672 (0.89%)	0.98	58				0.501	0	0	1	0
G15323A	A193T	Homoplasmy	1/115 (0.87%)	25/672 (3.72%)	0.23	58				0.517	0	0	1	0
A15326G	T194A	Homoplasmy	115/115 (100%)	672/672 (100%)	1	58				0.452	45	37	22	11
A15363G	N206S	Homoplasmy	1/115 (0.87%)	0	-	46				0.383	0	0	0	1
G15497A	G251S	Homoplasmy	1/115 (0.87%)	25/672 (3.72%)	0.23	56	Conserved		EXIT / Obesity	0.477	0	0	1	0
A15860G	I372V	Homoplasmy	1/115 (0.87%)	22/672 (3.27%)	0.27	29				0.238	0	0	1	0

**Somatic mutation** Novel mutations found in this study are shown in red.

\*1 The SNP frequency in persons with Parkinson's disease, Alzheimer's disease and type 2 diabetes w/ and w/o vascular lesion, men w/ and w/o juvenile obesity, and centenarians of Gifu and Tokyo in the database of GiiB-JST mTSN, the human mitochondrial genome SNP database (<http://mtnsp.>)

\*2 Calculated on the basis of the SNP frequency (C) in the database of GiiB-JST mTSN and the SNP frequency (T) in this study.

\*3 Data from MITOMAP database (<http://www.mitomap.org/MITOMAP>). PD: Parkinson's disease, AD: Alzheimer's disease, AMS: 4-Acetamido-4'-maleimidyl-distyrene-2,2'-disulphonic acid, DEAF: Maternally inherited DEAFness or aminoglycoside-induced DEAFness, DM: Type 2 diabetes mellitus, DMDF: Diabetes Mellitus + Deafness, EXIT: Exercise intolerance. HCM: Hypertrophic cardiomyopathy, LHON: Leber hereditary optic neuropathy, LDYT: Leber's hereditary optic neuropathy and DYSonia, MELAS: Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes, MS: Multiple sclerosis, NIDDM: Non-insulin-dependent diabetes mellitus,

\*4 Predicted pathogenicity score (Ref. 18). The amino acid variants showing more than 0.7 are considered as a high pathogenicity score group.



LgCa-176	80/M	Squamous cell carcinoma	T1N0M0	C3970T (L222L)	C5049T (L194L) G5147A (T226T)	G10310A (L84L)		C10976T (L73L) G11719A (G320G)	C12633T (S99S) C12882T (F182F)	G14476A (V66V)
LgCa-177	43/F	Squamous cell carcinoma	T1N0M0		A4769G (M100M) C4883T (P138P)	C10400T (T114T)		C11215T (Y152Y) G11719A (G320G)	C12705T (I123I)	C14668T (M2M)
LgCa-178	58/M	Squamous cell carcinoma	T1N1M0	C3546T (T80T) A4200T (L298L)	A4769G (M100M) C4883T (P138P)	C10400T (T114T)		T10873C (P38P) G11719A (G320G) G11719A (G320G)	C12705T (I123I)	
LgCa-179	54/F	Adenocarcinoma	T1N0M0		A4769G (M100M) C4883T (P138P)	C10400T (T114T)		T10873C (P38P) C11215T (Y152Y)	C12705T (I123I)	C14668T (M2M)
LgCa-180	68/M	Adenocarcinoma	T2N1M0	T4248C (I314I)	G4655A (T62T) A4769G (M100M)			G10801A (L14L) C11536T (Y259Y) C11647T (L296L) G11719A (G320G)	C12705T (I123I)	C14944T (I66I)
LgCa-181	64/M	Squamous cell carcinoma	T1N2M0		A4715G (G82G) A4769G (M100M)	C10400T (T114T)		T10873C (P38P) C11215T (Y152Y) G11719A (G320G)	C12705T (I123I)	C14668T (M2M)
LgCa-182	46/M	Adenocarcinoma	T1N2M0		A4769G (M100M) A4958G (M163M)	C10400T (T114T)		T10873C (P38P) T11017C (S86S) G11719A (G320G)	C12705T (I123I) G12771A (E145E)	G14364A (L104L)
LgCa-183	67/M	Squamous cell carcinoma	T2N0M0	T4117C (L271L)	A4769G (M100M) G4820A (E117E)			G11719A (G320G)	G13590A (L418L)	
LgCa-184	52/M	Pleomorphic carcinoma	T3N0M0		A4769G (M100M) G5231A (L254L) G5237A (P256P) G5417A (Q316Q)			G11719A (G320G)	G12372A (L12L) C12705T (I123I)	T15067C (F107F)
LgCa-187	73/M	Adenocarcinoma	T1N0M0	C3970T (L222L)	A4769G (M100M) C5049T (L194L) G5147A (T226T)	G10310A (L84L)		C10976T (L73L) G11719A (G320G)	C12633T (S99S) C12882T (F182F)	G14476A (V66V)
LgCa-188	59/M	Squamous cell carcinoma	T1N0M0		A4769G (M100M) C4883T (P138P)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12705T (I123I)	C14668T (M2M)
LgCa-189	73/M	Squamous cell carcinoma	T1N1M0	A3759G (L151L)	A4769G (M100M) C4883T (P138P) A5153G (L228L)	C10400T (T114T)		T10873C (P38P) T11569C (I270I) G11719A (G320G)	C12705T (I123I)	T14319C (N119N)
LgCa-190	62/M	Adenocarcinoma	T2N1M0		A4769G (M100M) G5147A (T226T) G5417A (Q316Q)	T10235C (A59A)		T10882C (F41F) G11719A (G320G)	C12705T (I123I)	A14233G (D147D)
LgCa-191	50/M	Adenocarcinoma	T2N2M0	C3846T (P180P)	A4769G (M100M)		C10607T (L46L)	G11719A (G320G)		
LgCa-192	54/F	Adenocarcinoma	T4N0M0	C3921T (S205S) T4248C (I314I)	A4769G (M100M)			C11536T (Y259Y) C11647T (L296L) G11719A (G320G)	C12705T (I123I)	G15172A (G142G)
LgCa-193	76/M	Squamous cell carcinoma	T1N0M0		A4769G (M100M) C4883T (P138P)			T10873C (P38P) C11215T (Y152Y) G11719A (G320G)	C12705T (I123I)	C14668T (M2M)
LgCa-194	41/M	Adenocarcinoma	T2N2M0		A4769G (M100M) C4883T (P138P) A5153G (L228L)	G10397A (W113W) C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12705T (I123I) C13029T (P231P) T13437C (P367P)	
LgCa-195	66/M	Bronchioalveolar carcinoma	T1N0M0		A4769G (M100M) C4883T (P138P)	C10400T (T114T)		T10873C (P38P) C11215T (Y152Y) G11719A (G320G)	C12705T (I123I)	C14668T (M2M)
LgCa-196	64/M	Adenocarcinoma	T1N0M0		C4625T (S52S) A4769G (M100M)			G11719A (G320G)	C12853T (L173L) T13437C (P367P)	G15346A (L200L)
LgCa-197	59/M	Bronchioalveolar carcinoma	T1N0M0		A4769G (M100M)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12705T (I123I)	T14308C (G122G)
LgCa-198	35/M	Squamous cell carcinoma	T?N1M0		A4769G (M100M) A4958G (M163M)	C10400T (T114T)		T10873C (P38P) T11017C (S86S) G11719A (G320G) T11722C (L321L)	C12705T (I123I) G12771A (E145E)	G14364A (L104L)
LgCa-199	63/M	Adenocarcinoma	T1N1M0		A4769G (M100M) G5231A (L254L) G5417A (Q316Q)			G11719A (G320G) A11731G (S324S)	G12372A (L12L) C12705T (I123I)	T14968C (N74N) T15067C (F107F)

										T14783C (L13L) G15043A (G99G) G15301A (L185L)
										T14783C (L13L) G15043A (G99G) G15301A (L185L)
										T14783C (L13L) G15043A (G99G) G15301A (L185L)
										C14944T (I66I)
A8188G (201G)		T9090C (S188S)								T14783C (L13L) G15043A (G99G) T15184C (I146I) G15301A (L185L)
										T14783C (L13L) G15043A (G99G) G15301A (L185L)
G8206A (M207M)										
										T15067C (F107F)
										T14783C (L13L) G15043A (G99G) G15301A (L185L)
										T14783C (L13L) G15043A (G99G) G15301A (L185L)
										A14893G (L49L)
									G8790A (88L)	G15043A (G99G)
										G15172A (G142G)
										T14783C (L13L) G15043A (G99G) G15301A (L185L)
										T14783C (L13L) G15043A (G99G) G15301A (L185L)
										T14783C (L13L) G15043A (G99G) G15301A (L185L)
										G15346A (L200L)
										T14783C (L13L) G15043A (G99G) G15301A (L185L)
										T14783C (L13L) G15043A (G99G) G15301A (L185L)
										T14968C (N74N) T15067C (F107F)

LgCa-200	58/F	Adenocarcinoma	T1N0M0	C4071T (Y255Y) A4164G (M286M)	A4769G (M100M) A5351G (L294L)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12405T (L23L) C12705T (I123I)	
LgCa-201	64/M	Adenocarcinoma	T1N0M0		A4769G (M100M) A4895G (M163M)			T11437C (A226A) G11719A (G320G)		
LgCa-202	76/M	Adenocarcinoma	T1N0M0		A4769G (M100M) T4859C (L130L) C4883T (P138P)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12705T (I123I)	T14635C (V13V) C14668T (M2M)
LgCa-205	74/F	Squamous cell carcinoma	T1N1M0		A4769G (M100M) C4883T (P138P)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12705T (I123I) T13656C (L440L)	C14668T (M2M)

\*1 TNM (Tumour/Node/Metastasis) classification for staging of cancer.

#### NSCLC metastases (37 cases)

Sample #	Histology	Metastatic site	None		Novel mutation					
			ND1	ND2	ND3	ND4L	ND4	ND5	ND6	
LuAdBrM-1	-	Adenocarcinoma	Brain		A4769G (M100M) A4958G (M163M)	C10400T (T114T)	G10646A (V59V)	T10873C (P38P) T11017C (S86S) G11719A (G320G)	C12705T (I123I) G12771A (E145E)	G14364A (L104L)
LuAdBrM-2	64/M	Adenocarcinoma	Brain		A4769G (M100M)	G10310A (L84L)		G11719A (G320G)	A14133G (L599L)	
LuAdBrM-3	-	Adenocarcinoma	Brain		A4769G (M100M) A4958G (M163M) G4991A (Q174Q)	C10400T (T114T)		T10873C (P38P) T11017C (S86S) G11719A (G320G) T11722C (L321L)	C12705T (I123I) G12771A (E145E)	G14364A (L104L)
LuAdBrM-4	-	Adenocarcinoma	Brain		G4655A (T62T) A4769G (M100M)			C11536T (Y259Y) C11647T (L296L) G11719A (G320G)	C12705T (I123I)	
LuAdBrM-5	79/M	Adenocarcinoma	Brain		A4769G (M100M)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12705T (I123I) T13015C (L227L)	T14308C (G122G)
LuAdBrM-6	-	Adenocarcinoma	Brain	G3483A (E59E)	G5231A (L254L) A4769G (M100M) G5417A (Q316G)			G11719A (G320G)	G12372A (L12L) C12705T (I123I) T13602C (Y422Y)	T15067C (F107F) G15301A (L185L)
LuAdBrM-7	49/M	Adenocarcinoma	Brain		A4769G (M100M)	A10403G (E115E)		G11719A (G320G)		
LuAdBrM-8	70/M	Adenocarcinoma	Brain		A4769G (M100M)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12705T (I123I)	T14308C (G122G)
LuAdBrM-9	-	Adenocarcinoma	Brain		A4769G (M100M) G5147A (T226T)	G10310A (L84L)		G11719A (G320G)	T13962C (L542L) A14133G (L599L)	
LuAdBrM-10	51/M	Adenocarcinoma	Brain		A4769G (M100M) C4883T (P138P)	C10400T (T114T)		T10873C (P38P) T11017C (S86S) G11719A (G320G)	C12705T (I123I)	C14668T (M2M)
LuAdBrM-11	-	Adenocarcinoma	Brain	G4140T (P278P)	A4769G (M100M)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12549 T (T71T) C12705T (I123I) A13152G (L272L)	
LuAdBrM-12	-	Adenocarcinoma	Brain		A4769G (M100M) A4895G (L130L)			T11437C (A226A) G11719A (G320G)	T13641C (P435P) A13887G (L517L)	
LuAdBrM-13	46/M	Adenocarcinoma	Brain		A4769G (M100M) C4883T (P138P)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12705T (I123I) A13104G (G256G) T13641C (P435P) A13887G (L517L)	C14668T (M2M)
LuAdBrM-14	-	Adenocarcinoma	Brain		A4769G (M100M) G5231A (L254L) G5417A (Q316G)			G11719A (G320G)	G12372A (L12L) G12651A (L105L) C12705T (I123I)	C14668T (M2M)
LuAdBrM-15	50/M	Adenocarcinoma	Brain		A4769G (M100M) A4958G (M163M)	C10400T (T114T)		T10873C (P38P) T11017C (S86S) G11719A (G320G) T11944C (L395L)	C12705T (I123I) G12771A (E145E)	
LuAdBrM-16	69/M	Adenocarcinoma	Brain		A4769G (M100M) C4883T (P138P)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12705T (I123I) A13104G (G256G)	G14364A (L104L)
LuAdBrM-17	50/F	Adenocarcinoma	Brain		A4769G (M100M) A4895G (M142M)			T11437C (A226A) G11719A (G320G)		

T7684C (L33L)		T14783C (L13L) G15043A (G99G) G15301A (L185L)
	C8829T (N101N)	C15223T (D159D)
		T14783C (L13L) G15043A (G99G) G15301A (L185L)
		T14783C (L13L) G15043A (G99G) T15139C (Y131Y) G15301A (L185L)

COII	ATP6	CYTB
		T14783C (L13L) G15043A (G99G) G15301A (L185L)
	C8844T (I106I)	G15346A (L200L)
		T14783C (L13L) G15301A (L185L)
		T14783C (L13L) G15301A (L185L)
		T15067C (F107F) G15301A (L185L)
		T14783C (L13L) G15043A (G99G) G15301A (L185L)
	G8856A (A110A)	G15346A (L200L)
		T14783C (L13L) G15043A (G99G) G15301A (L185L)
C7948T (Y121Y)	G8793C (P89P) G8856A (A110A)	T14783C (L13L) G15043A (G99G) G15301A (L185L)
	C8829T (N101N)	C15223T (D159D)
		T14783C (L13L) G15043A (G99G) G15301A (L185L)
		T15067C (F107F)
G7852A (E89E)		T14783C (L13L) G15043A (G99G) G15301A (L185L)
		T14783C (L13L) G15043A (G99G) G15301A (L185L)
	C8829T (N101N)	C15223T (D159D)



Colon cancer primary tissue (22 cases)

Case #	Age/Sex	Histology	TNM*1	None	Novel mutation					
				ND1	ND2	ND3	ND4L	ND4	ND5	ND6
ColoCa-1	69/M	Adenocarcinoma	T3N1M1	T4248C (I314I)	G4655A (T62T) A4769G (M100M)	G10325A (M89M)		T10873C (P38P) C11536T (Y259Y) C11647T (L296L) G11719A (G320G)	C12705T (I123I)	
ColoCa-2	65/M	Adenocarcinoma	T3N2M0		A4769G (M100M) A4793G (M108M) T5108C (T213T)	C10400T (T114T)		T10873C (P38P) G11719A (G320G) G11914A (T385T)	C12705T (I123I)	G14569A (S35S)
ColoCa-3	71/M	Adenocarcinoma	T3N1M0		A4769G (M100M) C4883T (P138P)	A10397G (W113W) C10400T (T114T)		T10873C (P38P) G11719A (G320G) A11746G (L329L) T11944C (L395L)	C12705T (I123I) A13278G (M315M)	
ColoCa-4	50/M	Adenocarcinoma	T4N4M0	C3970T (L222L)	A4769G (M100M) C5049T (L194L) G5147A (Q316C)	G10310A (L84L)		C10976T (L73L) G11719A (G320G)	C12633T (S99S) C12882T (F182F)	G14476A (V66V)
ColoCa-5	67/M	Adenocarcinoma	T4N4M0		A4769G (M100M) G5231A (L254L) G5237A (P256P) G5417A (Q316C)		T10724C (Y85Y)	G11719A (G320G)	G12372A (L12L) C12705T (I123I)	
ColoCa-6	67/F	Adenocarcinoma	P(T?N0M1) (Liver meta)		A4769G (M100M) C4883T (P138P)	C10400T (T114T)		T10873C (P38P) C11215T (Y152Y) G11719A (G320G)		C14668T (M2M)
ColoCa-7	52/F	Adenocarcinoma	T4N2M1 (Liver meta)		A4769G (M100M) C4883T (P138P)			T10873C (P38P) G11719A (G320G)	C12705T (I123I) A13104G (G256G) T13641C (P435P) A13887G (L517L)	C14668T (M2M)
ColoCa-8	61/M	Adenocarcinoma	T3N0M0	C3408T (R34R) T4248C (I314I)	A4769G (M100M)			G11719A (G320G)	C12705T (I123I) C14067T (T577T)	
ColoCa-9	66/M	Adenocarcinoma	T2N0M0	G4092A (K262K)	A4769G (M100M)			T10873C (P38P) G11719A (G320G)	C12705T (I123I)	
ColoCa-10	64/M	Adenocarcinoma	T3N0M0		A4769G (M100M) C4883T (P138P) A5153G (L228L)			T10873C (P38P) C11422T (V221V) G11719A (G320G)	C12705T (I123I) A14013G (E559E)	C14668T (M2M)
ColoCa-11	61/F	Adenocarcinoma	T3N1M0		A4769G (M100M) C4883T (P138P)			T10873C (P38P) C11215T (Y152Y) G11719A (G320G)		C14668T (M2M)
ColoCa-12	53/F	Adenocarcinoma	T3N1M0	G3882A (E192E) C4071T (Y255Y)	A4769G (M100M) C4850T (G127G)			T10873C (P38P) G11719A (G320G)	C12705T (I123I)	
ColoCa-13	66/M	Adenocarcinoma	T3N1M1 (Liver meta)	G3970T (L222L)	A4769G (M100M) C5049T (L194L) G5147A (T226T)	G10310A (L84L)		C10976T (L73L) G11719A (G320G)	C12633T (S99S) C12882T (F182F)	C14476A (V66V)
ColoCa-14	74/F	Adenocarcinoma	T1N0M0	C3970T (L222L)	A4769G (M100M) G4820A (E117E)			G11719A (G320G)		C14476A (V66V)
ColoCa-15	82/F	Adenocarcinoma	T1N0M0	C3495T (P63P) C4071T (Y255Y) A4164G (M286M)	A4769G (M100M) T5021C (I184I) A5351G (L294L)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12405T (L23L) C12705T (I123I) G13707A (L457L) C13782T (L482I)	
ColoCa-16	66/M	Carcinoid	T1N1M0		A4769G (M100M) C4883T (P138P)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12705T (I123I)	C14668T (M2M)
ColoCa-17	75/F	Adenocarcinoma	T1N0M0	C3970T (L222L)	A4769G (M100M)		T10535C (Y22Y) G10586A (S39S)	T10790C (L11L) G11719A (G320G)		
ColoCa-18	54/F	Adenocarcinoma	T4N1M1 (Liver meta)		A4769G (M100M) A5496C (M163M)	C10400T (T114T)		T10873C (P38P) T11017C (S86S) G11719A (G320G)	C12705T (I123I) G12771A (E145E)	G14364A (L104L) T14470C (G68G)
ColoCa-19	56/M	Adenocarcinoma	T3N0M0	G3531A (P75P)	A4769G (M100M) C4883T (P138P)	C10400T (T114T)		T10873C (P38P) G11719A (G320G)	C12705T (I123I) T12957C (N207N)	C14668T (M2M)

COIL	ATP6	CYTB
		T14783C (L13L) G15043A (G99G) G15301A (L185L)
C7867T (S94S) T8200C (S205S)		T14783C (L13L) G15043A (G99G) G15301A (L185L)
	A9180G (V218V)	T14783C (L13L) G15043A (G99G) G15301A (L185L)
		T15067C (F107F)
T7783C (L67L)		T14783C (L13L) G15043A (G99G) G15301A (L185L) A15874G (M376M)
		T14783C (L13L) G15043A (G99G) G15301A (L185L) C15518T (L258L)
C7747T (I55I)	A9180G (V218V)	T14783C (L13L) G15043A (G99G) G15301A (L185L) A15724G (W326W)
		T14783C (L13L) G15043A (G99G) G15301A (L185L)
		T14783C (L13L) G15043A (G99G) G15301A (L185L) A15874G (M376M)
		T14783C (L13L) G15043A (G99G) G15301A (L185L)
Matched case 1		
T7684C (L33L)		T14783C (L13L) A15043G (G99G) A15301G (L185L)
G8020A (P145P)	C8964T (T146T)	T14783C (L13L) G15043A (G99G) G15301A (L185L)
A7828G (L81L)		
		T14783C (L13L) G15043A (G99G) G15301A (L185L)
		T14783C (L13L) G15043A (G99G) G15301A (L185L)



ColoCa-20	62/M	Adenocarcinoma	T1N0M0		A4769G (M100M) G4820A (E117E) G5231A (L254L) G5417A (Q316Q)			G11719A (G320G)	C12705T (I123I) G12372A (L12L)				
ColoCa-21	63/M	Adenocarcinoma	T?N?M1 (Liver meta)		A4769G (M100M) A4958G (M163M)	C10400T (T114T)		T10873C (P38P) T11017C (S86S) G11719A (G320G)	C12705T (I123I) G12771A (E145E)	G14364A (L104L)			T14783C (L13L) G15043A (G99G) G15301A (L185L)
ColoCa-22	67/M	Adenocarcinoma	T4N1M1 (Liver meta)		A4769G (M100M) A5084G (L205L)	C10400T (T114T)		G11719A (G320G) G11914A (T385T)			Matched case 2	A9120G (L198L)	C15535T (N263N)

\*1 TNM (Tumour/Node/Metastasis) classification for staging of cancer.

Colon cancer metastases (11 cases)

Cae #	Age/Sex	Histology	Metastasis site	None		Novel mutation						
				ND1	ND2	ND3	ND4L	ND4	ND5	ND6		
CoAdBrM-1	-	Adenocarcinoma	Brain			C10400T (T114T)			G11719A (G320G)	C12882T (F182F)		
ColonLivM-1	-	-	Liver		A4958G (M163M)	C10400T (T114T)			T10873C (P38P) T11017C (S86S) G11719A (G320G)		G14364A (L104L)	
ColonLivM-2	-	-	Liver		C4883T (P138P)	C10104T (L16L) C10400T (T114T)			T10873C (P38P) G11719A (G320G)	C12705T (I123I)	T14287C (G129G) C14668T (M2M)	
ColonLivM-3	-	-	Liver		C4883T (P138P)	C10400T (T114T)			T10873C (P38P) G11719A (G320G)	C12705T (I123I) T12957C (N207N)	C14668T (M2M)	
ColonLivM-4	-	-	Liver		G5147A (T226T) G5417A (Q316Q)		C10607T (L46L)		T11465C (L236L) G11719A (G320G)	G12501A (M55M) C12705T (I123I) T13899C (Y562Y)		A14893G (L49L)
ColonLivM-5	-	-	Liver		T5108G (T29T)	C10400T (T114T)			T10873C (P38P) G11719A (G320G)	C12705T (I123I) A13563G (L409L)	T14200C (W158W) G14569A (S35S)	
ColonLivM-6	-	-	Liver		T4742C (N91N)				G11719A (G320G)			
ColoLivM-8	67/M	Adenocarcinoma	Liver		A4769G (M100M) A5084G (L205L)	C10400T (T114T)			G11719A (G320G) G11914A (T385T)			Matched case 2
ColoCa-13LivM	66/M	Adenocarcinoma	Liver	G3970T (L222L)	A4769G (M100M) C5049T (L194L) G5147A (T226T)	G10310A (L84L)			C10976T (L73L) G11719A (G320G)	C12633T (S99S) C12882T (F182F)	C14476A (V66V)	Matched case 1
ColonLuM-1	80/M	-	Lung			C10181T (F41F) C10400T (T114T)			T10873C (P38P) T11215T (Y152Y)		T14635C (V13V) C14668T (M2M)	
ColonLuM-2 (LgCa203)	71/F	Adenocarcinoma	Lung			C10400T (T114T)			T10873C (P38P) G11719A (G320G)		T14308C (G122G)	

COI1	ATP6	CYTB
		T14783C (L13L) G15043A (G99G) G15301A (L185L)
G8020A (P145P) G8251A (G222G)	C8964T (T146T)	T14783C (L13L) G15043A (G99G) G15301A (L185L)
		T14783C (L13L) G15043A (G99G) A15301A (L185L)
		A14893G (L49L)
G7600A (A5A)		T14783C (L13L) G15043A (G99G) G15301A (L185L)
C7909T (Y108Y)		G15346A (L200L) C15391T (S215S)
	A9120G (L198L)	C15535T (N263N)
G7672A (M19M) G8206A (M207M)		
G8206A (M207M)		
G8020A (P145P)		T14783C (L13L) G15043A (G99G) G15301A (L185L) A15874G (M376M)

Supplementary Table S4. Properties of synonymous SNPs and SNVs in *ND* genes in NSCLC and colon cancer clinical samples.

Novel mutation

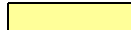
SNP/Mutation	Amino acid	Frequency T (this study) (%)	Frequency C (mtSNP-Japan)*1 (%)	Frequency (T/C)	No. of cases detected			
					NSCLC		Colon Cancer	
					Primary (N=45)	Metastases (N=37)	Primary (N=22)	Metastases (N=11)
<b>ND1</b>								
C3408T	R34R	1/115 (0.87%)	0	-	0	0	1	0
G3483A	E59E	1/115 (0.87%)	0	-	0	1	0	0
C3495T	P63P	1/115 (0.87%)	0	-	0	0	1	0
G3531A	P75P	2/115 (1.74%)	3/672 (0.45%)	3.87	1	0	1	0
C3546T	T80T	1/115 (0.87%)	2/672 (0.30%)	2.9	1	0	0	0
T3552A	A82A	1/115 (0.87%)	1/672 (0.15%)	5.8	0	1	0	0
A3759G	L151L	1/115 (0.87%)	5/672 (0.74%)	1.18	1	0	0	0
T3826C	L174L	1/115 (0.87%)	1/672 (0.15%)	5.8	0	1	0	0
C3846T	P180P	1/115 (0.87%)	0	-	1	0	0	0
G3882A	E192E	2/115 (1.74%)	4/672 (0.60%)	2.9	0	1	1	0
C3921T	S205S	2/115 (1.74%)	0	-	2	0	0	0
C3970T	L222L	8/115 (6.96%)	40/672 (5.95%)	1.17	2	3	3 (1 w/ meta)	0
C4071T	Y255Y	7/115 (6.09%)	34/672 (5.06%)	1.2	3	2	2	0
T4117C	L271L	4/115 (3.48%)	15/672 (2.23%)	1.56	1	1	0	2
G4140T	P278P	2/115 (1.74%)	4/672 (0.60%)	2.9	1	1	0	0
A4164G	M286M	5/115 (4.35%)	30/672 (4.46%)	0.98	3	1	1	0
A4200T	L298L	1/115 (0.87%)	2/672 (0.30%)	2.9	1	0	0	0
T4248C	I314I	7/115 (6.09%)	50/672 (7.44%)	0.82	3	2	2 (1 w/ meta)	0
<b>ND2</b>								
C4505T	T12T	1/115 (0.87%)	9/672 (1.34%)	0.65	1	0	0	0
C4625T	S52S	2/115 (1.74%)	1/672 (0.15%)	11.6	1	1	0	0
G4655A	T62T	4/115 (3.48%)	39/672 (5.80%)	0.6	1	2	1 w/ meta	0
A4715G	G82G	2/115 (1.74%)	20/672 (2.98%)	0.34	1	1	0	0
T4742C	N91N	3/115 (2.61%)	4/672 (0.60%)	4.35	0	2	0	1
A4769G	M100M	115/115 (100%)	672/672 (100.00%)	1	45	37	22 (7 w/ meta)	11
A4793G	M108M	1/115 (0.87%)	22/672 (3.27%)	0.27	0	0	1	0
G4820A	E117E	6/115 (5.22%)	20/672 (2.98%)	1.75	2	1	2	1
C4850T	G127G	2/115 (1.74%)	4/672 (0.60%)	2.9	0	1	1	0
T4856C	L129L	1/115 (0.87%)	0	-	0	1	0	0
T4859C	L130L	2/115 (1.74%)	12/672 (1.79%)	0.97	1	1	0	0
C4883T	P138P	35/115 (30.43%)	260/672 (38.69%)	0.79	17	9	7 (2 w/ meta)	2
A4895G	M142M	3/115 (2.61%)	13/672 (1.93%)	0.9	1	2	0	0
A4958G	M163M	11/115 (9.57%)	46/672 (6.85%)	1.4	5	4	1 w/ meta	1
G4991A	Q174Q	1/115 (0.87%)	1/672 (0.15%)	5.8	0	1	0	0
T5021C	I184I	2/115 (1.74%)	2/672 (0.30%)	5.8	1	0	1	0
C5049T	L194L	7/115 (6.09%)	15/672 (2.23%)	2.73	2	2	2 (1 w/ meta)	1
T5108C	T213T	3/115 (2.61%)	63/672 (9.38%)	0.28	1	0	1	1
G5147A	T226T	10/115 (8.70%)	41/672 (6.10%)	1.43	3	4	2 (1 w/ meta)	1
A5153G	L228L	4/115 (3.48%)	10/672 (1.49%)	2.34	2	1	1	0
G5231A	L254L	7/115 (6.09%)	38/672 (5.65%)	1.08	3	2	2	0
G5237A	P256P	2/115 (1.74%)	4/672 (0.60%)	2.92	1	0	1	0
G5261A	W264W	1/115 (0.87%)	4/672 (0.60%)	1.45	1	0	0	0
T5291C	N274N	1/115 (0.87%)	0	-	1	0	0	0
A5351G	L294L	5/115 (4.35%)	30/672 (4.46%)	0.98	3	1	1	0

G5417A	Q316Q	10/115 (8.70%)	55/672 ( 8.18%)	1.06	5	2	2	1
<b>ND3</b>								
C10104T	L16L	1/115 (0.87%)	14/672 ( 2.08%)	0.42	0	0	0	1
C10181T	F41F	1/115 (0.87%)	18/672 ( 2.68%)	0.32	0	0	0	1
T10235C	A59A	1/115 (0.87%)	2/672 ( 0.30%)	2.9	1	0	0	0
T10238C	I60I	1/115 (0.87%)	12/672 ( 1.79%)	0.49	1	0	0	0
G10310A	L84L	9/115 (7.83%)	50/672 ( 7.44%)	1.05	2	5	2 (1 w/ meta)	0
G10325A	M89M	1/115 (0.87%)	1/672 ( 0.15%)	5.8	0	0	1 w/ meta	0
A10397G	W113W	2/115 (1.74%)	29/672 ( 4.32%)	0.4	1	0	1	0
C10400T	T114T	54/115 (46.96%)	441/672 (65.62%)	0.72	21	18	8	7
A10403G	E115E	1/115 (0.87%)	1/672 ( 0.15%)	5.8	0	1	0	0
<b>ND4L</b>								
T10535C	Y22Y	1/115 (0.87%)	2/672 ( 0.30%)	2.9	0	0	1	0
G10586A	S39S	1/115 (0.87%)	2/672 ( 0.30%)	2.9	0	0	1	0
C10607T	L46L	2/115 (1.74%)	18/672 ( 2.68%)	0.65	1	0	0	1
G10646A	V59V	2/115 (1.74%)	6/672 ( 0.89%)	1.96	1	1	0	0
T10724C	Y85Y	1/115 (0.87%)	0	-	0	0	1	0
<b>ND4</b>								
T10790C	L11L	1/115 (0.87%)	4/672 ( 0.60%)	1.45	0	0	1	0
G10801A	L14L	2/115 (1.74%)	4/672 ( 0.60%)	2.9	2	0	0	0
T10873C	P38P	66/115 (57.39%)	440/672 (65.48%)	0.88	28	18	14 (5 w/ meta)	6
T10882C	F41F	1/115 (0.87%)	0	-	1	0	0	0
C10976T	L73L	6/115 (5.22%)	19/672 ( 2.83%)	1.84	2	1	2 (1 w/ meta)	1
A11017C	S86S	13/115 (11.30%)	38/672 ( 5.65%)	2	5	7	1	0
A11023G	P88P	1/115 (0.87%)	0	-	1	0	0	0
C11215T	Y152Y	9/115 (7.83%)	31/672 ( 4.61%)	1.7	6	0	2 (1 w/ meta)	1
A11239G	L160L	1/115 (0.87%)	0	-	1	0	0	0
T11260C	T167T	1/115 (0.87%)	0	-	1	0	0	0
C11389T	Y210Y	1/115 (0.87%)	1/672 ( 0.15%)	5.8	0	1	0	0
C11422T	V221V	1/115 (0.87%)	1/672 ( 0.15%)	5.8	0	0	1	0
T11437C	A226A	3/115 (2.61%)	5/672 ( 0.74%)	3.53	1	2	0	0
T11465C	L236L	1/115 (0.87%)	0	-	0	0	0	1
C11536T	Y259Y	7/115 (6.09%)	43/672 ( 6.40%)	0.95	4	2	1 w/ meta	0
T11569C	I270I	1/115 (0.87%)	1/672 ( 0.15%)	5.8	1	0	0	0
C11647T	L296L	6/115 (5.22%)	39/672 ( 5.80%)	0.9	3	2	1 w/ meta	0
C11665T	L302L	1/115 (0.87%)	4/672 ( 0.60%)	1.45	0	1	0	0
G11719A	G320G	111/115 (96.52%)	671/672 (99.85%)	0.97	44	36	22 (7 w/ meta)	9
T11722C	L321L	2/115 (1.74%)	6/672 ( 0.89%)	1.96	1	1	0	0
A11731G	S324S	1/115 (0.87%)	0	-	1	0	0	0
A11746G	L329L	1/115 (0.87%)	1/672 ( 0.15%)	5.8	0	0	1	0
G11914A	T385T	4/115 (3.48%)	37/672 ( 5.51%)	0.63	0	2	2 (1 w/ meta)	0
T11944C	L395L	2/115 (1.74%)	17/672 ( 2.53%)	0.69	0	1	1	0
G12007A	W416W	1/115 (0.87%)	4/672 ( 0.60%)	1.45	1	0	0	0
C12088T	P443P	2/115 (1.74%)	2/672 ( 0.30%)	5.8	1	1	0	0
T12091T	I444I	1/115 (0.87%)	4/672 ( 0.60%)	1.45	0	1	0	0
<b>ND5</b>								
A12358G	T8T	1/115 (0.87%)	0	-	1	0	0	0
G12372A	L12L	8/115 (6.96%)	38/672 (5.65%)	1.23	4	2	2	0
C12405T	L23L	5/115 (4.35%)	29/672 (4.32%)	1.01	3	1	1	0
G12501A	M55M	1/115 (0.87%)	10/672 ( 1.49%)	0.58	0	0	0	1
C12549T	T71T	2/115 (1.74%)	4/672 (0.60%)	2.9	1	1	0	0

C12633T	S99S	7/115 (6.09%)	18/672 (2.68%)	2.13	2	2	2 (1 w/ meta)	1
G12651C	L105L	3/115 (2.61%)	2/672 (0.30%)	8.7	1	2	0	0
C12705T	I123I	81/115 (70.43%)	545/672 (81.10%)	0.87	38	23	15 (4 w/ meta)	5
T12714C	I126I	1/115 (0.87%)	0	-	0	1	0	0
G12771A	E145E	11/115 (9.57%)	47/672 (6.99%)	1.37	5	4	2 (1 w/ meta)	0
C12853T	L173L	2/115 (1.74%)	1/672 (0.15%)	11.6	1	1	0	0
C12882T	F182F	9/115 (7.83%)	35/672 (5.21%)	1.5	2	3	2 (1 w/ meta)	2
T12957C	N207N	3/115 (2.61%)	4/672 (0.60%)	4.35	1	0	1	1
T13015C	L227L	1/115 (0.87%)	0	-	0	1	0	0
C13029T	P231P	1/115 (0.87%)	1/672 (0.15%)	5.8	1	0	0	0
A13104G	G256G	3/115 (2.61%)	21/672 (3.12%)	0.84	0	2	1 w/ meta	0
A13152G	L272L	2/115 (1.74%)	4/672 (0.60%)	2.9	1	1	0	0
A13263G	Q309Q	1/115 (0.87%)	2/672 (0.30%)	2.9	0	1	0	0
A13278G	M315M	1/115 (0.87%)	8/672 (1.19%)	0.73	0	0	1	0
T13437C	P367P	3/115 (2.61%)	4/672 (0.60%)	4.35	2	1	0	0
A13563G	L409L	3/115 (2.61%)	32/672 (4.76%)	0.37	2	0	0	1
G13590A	L418L	4/115 (3.48%)	19/672 (2.83%)	1.23	2	1	0	1
T13602C	Y422Y	1/115 (0.87%)	2/672 (0.30%)	2.9	0	1	0	0
T13641C	P435P	3/115 (2.61%)	0	-	0	2	1 w/ meta	0
T13656C	L440L	2/115 (1.74%)	1/672 (0.15%)	11.6	2	0	0	0
G13707A	L457L	1/115 (0.87%)	0	-	0	0	1	0
C13782T	I482I	1/115 (0.87%)	0	-	0	0	1	0
A13887G	L517L	3/115 (2.61%)	4/672 (0.60%)	4.35	0	2	1 w/ meta	0
T13899C	Y562Y	1/115 (0.87%)	0	-	0	0	0	1
T13962C	L542L	2/115 (1.74%)	0	-	0	2	0	0
A14013G	E559E	1/115 (0.87%)	2/672 (0.30%)	2.9	0	0	1	0
C14067T	T577T	1/115 (0.87%)	0	-	0	0	1	0
A14133G	L599L	3/115 (2.61%)	12/672 (1.79%)	1.46	0	3	0	0
<b>ND6</b>								
T14200C	W158W	2/115 (1.74%)	30/672 (4.46%)	0.39	1	0	0	1
A14233G	D147D	1/115 (0.87%)	0	-	1	0	0	0
C14281T	G131G	1/115 (0.87%)	9/672 (1.34%)	0.65	1	0	0	0
T14287C	G129G	1/115 (0.87%)	10/672 (1.49%)	0.58	0	0	0	1
T14308C	G122G	4/115 (3.48%)	11/672 (1.64%)	2.12	1	2	0	1
T14319C	N119N	1/115 (0.87%)	0	-	1	0	0	0
G14364A	L104L	12/115 (10.43%)	42/672 (6.25%)	1.67	5	4	2 w/ meta	1
T14374C	V100V	1/115 (0.87%)	0	-	1	0	0	0
T14386C	L96L	1/115 (0.87%)	1/672 (0.15%)	5.8	1	0	0	0
A14464G	T70T	1/115 (0.87%)	0	-	1	0	0	0
T14470C	G68G	1/115 (0.87%)	29/672 (4.32%)	0.2	0	0	1 w/ meta	0
G14476A	V66V	7/115 (6.09%)	19/672 (2.83%)	2.15	2	2	3 (1 w/ meta)	0
G14569A	S35S	3/115 (2.61%)	64/672 (9.52%)	0.27	1	0	1	1
A14587G	G29G	1/115 (0.87%)	0	-	1	0	0	0
A14605G	P23P	2/115 (1.74%)	29/672 (4.32%)	0.23	0	2	0	0
T14635C	V13V	2/115 (1.74%)	0	-	1	0	0	1
C14668T	M2M	32/115 (27.83%)	237/672 (35.27%)	0.79	15	8	6 (2 w/ meta)	3

SNP/Mutation	Amino acid	Frequency T (this study) (%)	Frequency C (mSNP-Japan)*1 (%)	Frequency (T/C)	No. of cases detected			
					NSCLC		Colon Ca	
					Primary (N=45)	Metastases (N=37)	Primary (N=22)	Metastases (N=11)
<b>COII</b>								
G7600A	A5A	2/115 (0.87%)	32/672 (4.76%)	0.18	1	0	0	1
G7672A	M19M	1/115 (0.87%)	0	-	0	0	0	1
T7684C	L33L	4/115 (3.48%)	29/672 (4.32%)	0.81	3	1	1	0
G7702A	L39L	1/115 (0.87%)	0	-	0	1	0	0
T7738C	T51T	1/115 (0.87%)	2/672 (0.30%)	2.9	0	1	0	0
T7741C	N52N	1/115 (0.87%)	0	-	0	1	0	0
C7747T	I55I	1/115 (0.87%)	0	-	0	0	1	0
T7783C	L67L	1/115 (0.87%)	0	-	0	0	1 w/ meta	0
A7828G	L81L	1/115 (0.87%)	2/672 (0.30%)	2.9	0	0	1	0
G7852A	E89E	1/115 (0.87%)	1/672 (0.15%)	5.8	0	1	0	0
C7867T	S94S	1/115 (0.87%)	25/672 (3.72%)	0.23	0	0	1	0
C7909T	Y108Y	2/115 (0.87%)	5/672 (0.74%)	1.18	0	1	0	1
C7948T	Y121Y	1/115 (0.87%)	2/672 (0.30%)	2.9	0	1	0	0
A7960G	P125P	1/115 (0.87%)	4/2704 (0.15%)	5.8	0	1	0	0
G8020A	P145P	6/115 (5.22%)	1/672 (0.15%)	34.8	1	2	1	2
T8167A	G194G	1/115 (0.87%)	84/672 (12.50%)	0.07	0	1	0	0
T8200C	S205S	1/115 (0.87%)	1/672 (0.14%)	6.2	0	0	1	0
G8206A	M207M	4/115 (3.48%)	25/672 (3.72%)	0.94	1	1	0	2
G8251A	G222G	1/115 (0.87%)	15/672 (2.23%)	0.39	0	0	0	1
<b>ATP6</b>								
T8598C	I24I	1/115 (0.87%)	0	-	1	0	0	0
T8614C	L30L	2/115 (0.87%)	1/672 (0.15%)	5.8	1	1	0	0
A8697G	M57M	1/115 (0.87%)	0	-	1	0	0	0
A8700G	M58M	1/115 (0.87%)	0	-	1	0	0	0
A8706G	M60M	1/115 (0.87%)	0	-	1	0	0	0
T8793C	P89P	2/115 (0.87%)	4/672 (0.60%)	1.45	1	1	0	0
C8829T	N101N	4/115 (3.48%)	25/672 (3.72%)	0.94	1	3	0	0
C8844T	I106I	1/115 (0.87%)	3/672 (0.45%)	1.93	0	1	0	0
G8856A	A110A	4/115 (3.48%)	5/672 (0.74%)	4.7	1	3	0	0
C8964T	T146T	5/115 (4.35%)	61/672 (9.08%)	0.48	1	2	1	1
A9120G	L198L	2/115 (0.87%)	1/672 (0.14%)	6.21	0	0	1 w/ meta	1
T9165C	V213V	1/115 (0.87%)	7/672 (1.04%)	0.84	1	0	0	0
A9180G	V218V	4/115 (3.48%)	27/672 (4.02%)	0.87	2	0	2	0
<b>CYT6</b>								
T14783C	L13L	65/115 (56.52%)	441/672 (65.62%)	0.86	29	18	13 (4 w/ meta)	5
A14893G	L49L	2/115 (0.87%)	18/672 (2.68%)	0.32	1	0	0	1
C14944T	I66I	2/115 (0.87%)	28/672 (4.17%)	0.21	2	0	0	0
T14968C	N74N	1/115 (0.87%)	21/672 (3.13%)	0.28	1	0	0	0
C15040T	I98I	1/115 (0.87%)	4/672 (0.60%)	1.45	1	0	0	0
A15043G	G99G	64/115 (55.65%)	442/672 (65.77%)	0.85	30	16	13 (3 w/ meta)	5
T15067C	F107F	6/115 (5.22%)	23/672 (3.42%)	1.53	3	2	1	0
G15106A	L120L	1/115 (0.87%)	3/672 (0.45%)	1.93	1	0	0	0
T15139C	Y131Y	2/115 (0.87%)	1/672 (0.15%)	5.8	2	0	0	0
G15148A	P134P	1/115 (0.87%)	6/672 (0.89%)	0.98	0	1	0	0
G15172A	G142G	1/115 (0.87%)	1/672 (0.15%)	5.8	1	0	0	0
T15184C	I146I	1/115 (0.87%)	6/672 (0.89%)	0.98	1	0	0	0

C15223T	D159D	4/115 (3.48%)	25/672 (3.72%)	0.94	1	3	0	0
A15301G	L185L	66/115 (57.39%)	441/672 (65.63%)	0.87	29	19	13 (4 w/ meta)	5
G15346A	L200L	7/115 (6.09%)	21/672 (3.13%)	1.95	1	5	0	1
C15391T	S215S	1/115 (0.87%)	3/672 (0.45%)	1.93	0	0	0	1
C15518T	L258L	1/115 (0.87%)	16/672 (2.38%)	0.37	0	0	1 w/ meta	0
C15535T	N263N	2/115 (0.87%)	21/672 (3.13%)	0.28	0	0	1 w/ meta	1
A15724G	W326W	1/115 (0.87%)	10/672 (1.49%)	0.58	0	0	1	0
A15874G	M376M	3/115 (2.61%)	23/672 (3.42%)	0.76	0	0	2 (1 w/ meta)	1



Somatic mutation. Novel mutations are shown in red.

\*1 GiiB-JST mtSN: human mitochondrial genome single nucleotide polymorphism database (<http://mitsnp.tmig.or.jp/>). SNP frequency in patients with Parkinson's disease, Alzheimer's disease, type 2 diabetes w/ and w/o vascular lesion, men w/ and w/o juvenile obese, and centenarians of Gifu and Tokyo.

Supplementary Table S5. Nonsynonymous SNPs and SNVs in the *ND* genes selected to evaluate the association with distant metastasis in NSCLC and colon cancer.

Gene	SNP/ Mutation*1	Amino acid substitution	Homoplasmy or heteroplasmy	Frequency (T/C)*2	Grantham value	Evolutionary conservation of the original amino acid	Conformational change	Reported disease association*3	MutPred Pathogenicity Score*4	No. of cases detected							
										NSCLC		Colon Cancer		Lung adenocarcinoma		Colon adenocarcinoma	
										Primary (n=45)	Metastases (n=37)	Primary (n=22)	Metastases (n=11)	Primary (n=45)	Metastases (n=37)	Primary (n=22)	Metastases (n=11)
	T3394C	Y30H	Homoplasmy	2.09	83	Conserved		LHON / Diabetes / CPT deficiency / high altitude adaptation	0.783	1	3	1 w/ distant meta	0	0	3	1 w/ distant meta	0
	T3398C	M31T	Homoplasmy	2.9	81	Conserved		DMDF+HCM / GDM / possibly LVNC cardiomyopathy- associated	0.751	0	0	1	0	0	0	0	0
ND1	C3497T	A64V	Homoplasmy	2.04	64		Yes	LHON	0.413	1	5	0	1	1	5	0	0
	C3689G	A128G	Homoplasmy	-	60		Yes		0.747	0	1	0	1	0	1	0	1
	G3709A	A135T	Heteroplasmy or Heterogeneous	-	58	Conserved	Yes		0.774	1	0	0	0	0	0	0	0
	G3955A	A217T	Heteroplasmy or Heterogeneous	-	58		Yes		0.736	0	0	0	1	0	0	0	0
ND3	T10363C	L102P	Heteroplasmy or Heterogeneous	-	98	Conserved			0.746	0	1	0	0	0	1	0	0
ND4	C11409T	P217L	Heteroplasmy or Heterogeneous	-	98	Conserved			0.83	0	1	0	0	0	1	0	0
	T12338C	M1T	Homoplasmy	3	81	Conserved		DEAF1555 increased penetrance / LHON	0.966	0	0	1	0	0	0	1	0
	C12813A	Y159STOP	Heteroplasmy or Heterogeneous	-	-		Truncated		-	0	1	0	0	0	1	0	0
ND5	G13103A	G256E	Heteroplasmy or Heterogeneous	-	98	Conserved			0.834	1	0	0	0	0	0	0	0
	G13366A	G344STOP	Heteroplasmy or Heterogeneous	-	-		Truncated		-	0	0	1 (same case)	0	0	0	1 (same case)	0
	T14138C	L601P	Homoplasmy	-	98	Conserved			0.762	0	0	0	1	0	0	0	1
ND6	14504delA	L57STOP	Homoplasmy	-	-		Truncated		-	0	0	1 (same case)	0	0	0	1 (same case)	0

\*1 Novel mutations found in this study are shown in red.

\*2 Calculated on the basis of the SNP frequency (C) in persons with Parkinson's disease, Alzheimer's disease and type 2 diabetes w/ and w/o vascular lesion and men w/ and w/o juvenile obese, and centenarians of Gifu and Tokyo in the database of GiIB-JST mtSN; human mitochondrial genome single nucleotide polymorphism database (<http://mitsnp.tmg.or.jp/>) and the SNP frequency (T) in this study.

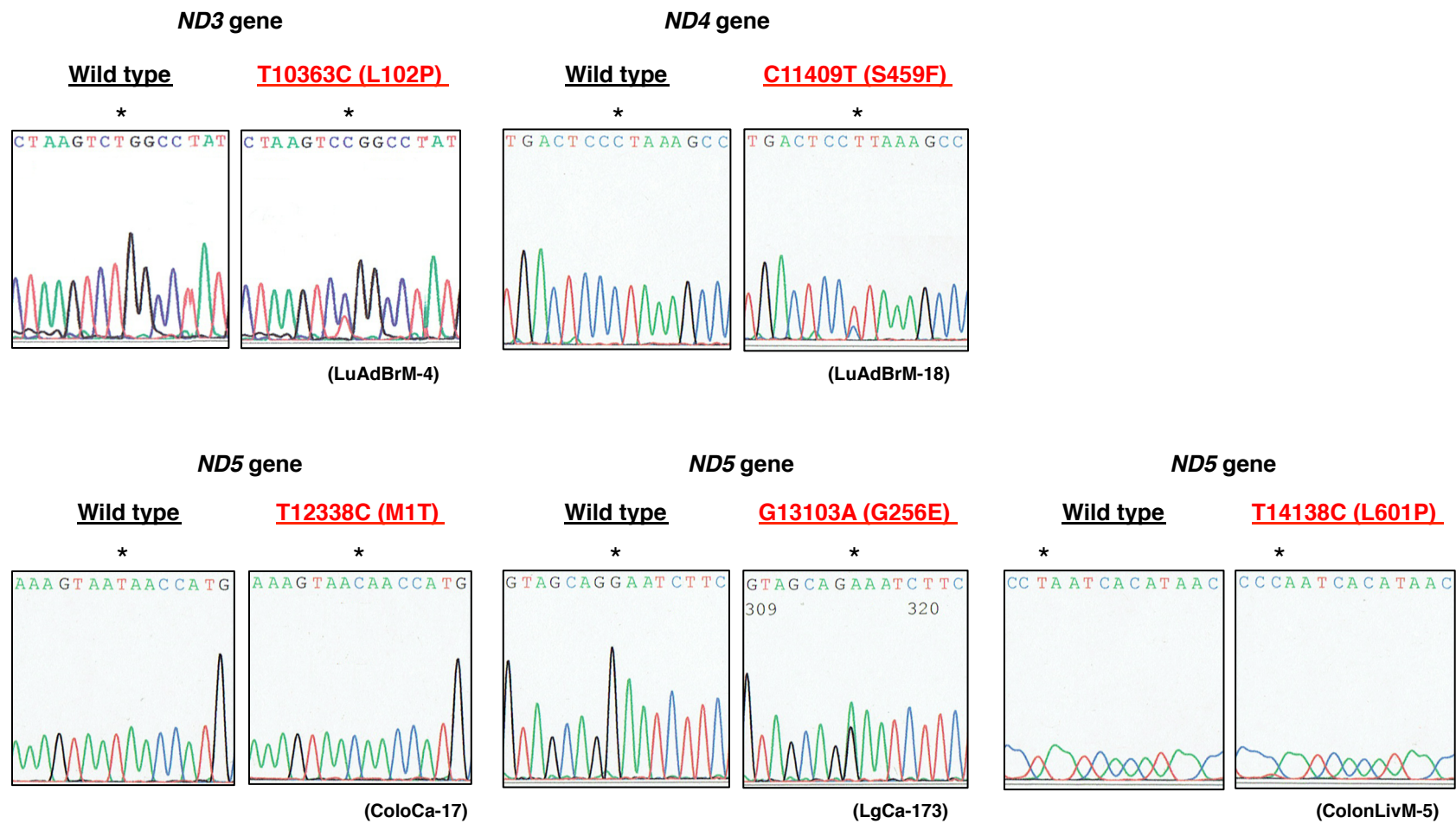
\*3 Data from MITOMAP database (<http://www.mitomap.org/MITOMAP>). LHON; Leber hereditary optic neuropathy, CPT; Carnitine Palmitoyltransferase, DMDF; Diabetes mellitus + Deafness, HCM; Hypertrophic cardiomyopathy, GDM; Gestational diabetes mellitus, LVNC; Left ventricular noncompaction.

\*4 Predicted pathogenicity score (Ref. 18). The amino acid variants showing more than 0.7 are considered as a high pathogenicity score group.

**Supplementary Table S6. PCR primers used for sequencing and qPCR.**

Primer	Sequence (5'-3')	Accession No.	Application		
ND1-1F	AACAGGGTTTGTAAAGATGGC	NC_005089.1	Sequencing		
ND1-1R	GGTTCGATTCTCATAGTCCTA				
ND1-2F	CATCAAACCTCAAACCTACGCCCT				
ND1-2R	TTCGGTTGGTCTCTGCTAGT				
ND2-1F	ATGAGAATCGAACCCTATCCC				
ND2-1R	TAAGATTTTGCCTAGCTGGGT				
ND2-2F	GACATCCGGCCTGCTTCTT				
ND2-2R	GAGTGGGGTTTTGCAGTCC				
ND3-ND4L-F	CCATCTATTGATGAGGGTCTT				
ND3-ND4L-R	ATAATTAGGCTGTGGGTGGTT				
ND4-1F	CTAGTATATCGCTCACACCTCA				
ND4-1R	GCTTCGACATGGGCTTTAGGGA				
ND4-2F	CTACTCACTCTCACTGCCCAAG				
ND4-2R	GGGAATTAGGGAAGTCAGGGT				
ND5-1F	CTCACAAGAAGTCTAACTCATGCC				
ND5-1R	CTAGTAGTGGGGTGAGGCTTGATTA				
ND5-2F	CATCGGCTGAGAGGGCGTAGGAAT				
ND5-2R	GAGAGTAATAGATAGGGCTCAGGCG				
ND5-3F	CTCCGGGTCCATCATCCACAACCT				
ND5-3R	GATCCTATTGGTGCGGGGGCTTTG				
ND6-F	CAATTTACAGCACCAATCTCCA				
ND6-R	TATTAGGGGGTTAGTTTTGCG				
COII-F	ACACATTCTGAAGAACCCTAT				
COII-R	TTTAGTTGGGGCATTCTACTG				
ATP6-F	TAAATACTACCGTATGGCCCA				
ATP6-R	CGTTATGGAGTGGAAGTGAAA				
CYTB-F1	ACTAAACCCACACTCAACAGAAAG				
CYTB-F2	GTCATTAAGGAGAGAAGG				
CYTB-F2	ATACATTGGGACAGACCTAGTTC				
CYTB-R2	CTTTGGGTGCTAATGGTGGAGT				
HIF1a-F	CCATGCCCCAGATTCAAGATCA			NM_001313919.1	qPCR
HIF1a-R	TCACTGGGACTGTTAGGCTGG				
Pdh1a-F	CCTCCCTTTGAAGTGCCTGG	M76727.1			
Pdh1a-R	AGCACAGAGTTCCTTACGCT				
Pdhb-F	AAAGGCAAGGGACCCACATC	NM_024221			
Pdhb-R	TGGCTTCGATGTCCATTGGT				
Pdk1-F	AGGATCGGTTATGCCAACTGT	NM_172665			
Pdk1-R	AACCAGGAACCTCACACCCC				
MMP11-F	CACCGTCATCACCCCTGTGAA	NM_008606.3			
MMP11-R	GGTTCGGGCATTTCAGTACA				
Plaur-F	ACTACCGTGCTTCGGGAATG	NM_011113.4			
Plaur-R	GCCTGTTGCAGAGGTTTGTG				
Cel7-F	GATCTCTGCCACGCTTCTGT	NM_013654			
Cel7-R	ATAGCCTCCTCGACCCACTT				
CD44-F	AGAAGAGCACCCCAGAAAGC	CT010324.1			
CD44-R	TCTGAAACCACGTCTCCTGC				
Kras-F	GCGCTGACCTAGGGAATGTT	NM_021284.6			
Kras-R	TCACTTCACAGCACGTACTCC				
Myc-F	ACAGTGTTCTCTGCCTCTGC	NM_001177352			
Myc-R	GCTGTACGGAGTCGTAGTCG				
Gapdh-F	TGCACCACCAACRGCTTAG	NM_008084			
Gapdh-R	GGATGCAGGGATGATGTTT				





**Supplementary Fig. S1.** Selected SNVs found in the clinical samples.

### T10363C

<b>ND3 a.a. sequences</b>	98	101	102	108	118
<i>Homo sapiens</i>	MSSLLLIIL ALS	<b>L</b>	AYEWLQ	KGLDWTE	
<b>LuAdBrM-4 (L102P)</b>	MSSLLLIIL ALS	<b>P</b>	AYEWLQ	KGLDWTE	
<i>Mus musculus</i>	IMAFILVTIL SLG	<b>L</b>	AYEWTQ	KGLEWTE	
<i>Bos taurus</i>	TMALFLIILL AVS	<b>L</b>	AYEWTQ	KGLEWTE	
<i>Gallus gallus</i>	TWATIIALL TFG	<b>L</b>	IYEWLQ	GGLEWAE	
<i>Xenopus laevis</i>	LWAALILTLL TLG	<b>L</b>	IYEWLQ	GGLEWAE	
<i>Salmo salar</i>	AWSAAVLALL TLG	<b>L</b>	IYEWLQ	GGLEWAE	
<i>Drosophila melanogaster</i>	ITSIIFILIL LIG	<b>L</b>	YHEWNQ	GMLNWSN	

### G13103A (G256E)

<b>ND5 a.a. sequences</b>	252	255	256	262	272
<i>Homo sapiens</i>	VSALLHSSTM VVA	<b>G</b>	IFLLIR	FHPLAENSPL	
<b>LgCa-173 (G256E)</b>	VSALLHSSTM VVA	<b>E</b>	IFLLIR	FHPLAENSPL	
<i>Mus musculus</i>	VSALLHSSTM VVA	<b>G</b>	IFLLVR	FHPLTTNNF	
<i>Bos taurus</i>	VSALLHSSTM VVA	<b>G</b>	IFLLIR	FYPLTENNKY	
<i>Gallus gallus</i>	VSALLHSSTM VVA	<b>G</b>	IFLLIR	THPFLSSNKT	
<i>Xenopus laevis</i>	VSALLHSSTM VVA	<b>G</b>	IFLLIR	ISPMMNNQT	
<i>Salmo salar</i>	VSALLHSSTM VVA	<b>G</b>	IFLLIR	LHPLMENNQT	
<i>Drosophila melanogaster</i>	VSALVHSSTL VTA	<b>G</b>	VYLLIR	FNIILSTSWL	

### C11409T

<b>ND4 a.a. sequences</b>	213	216	217	223	233
<i>Homo sapiens</i>	MVKMPYGLH LWL	<b>P</b>	KAHVEA	PIAGSMVLAA	
<b>LuAdBrM-18 (P217L)</b>	MVKMPYGLH LWL	<b>L</b>	KAHVEA	PIAGSMVLAA	
<i>Mus musculus</i>	LIKMPYGVH LWL	<b>P</b>	KAHVEA	PIAGSMILAA	
<i>Bos taurus</i>	MVKMPYGLH LWL	<b>P</b>	KAHVEA	PIAGSMVLAA	
<i>Gallus gallus</i>	MVKAPYGLH LWL	<b>P</b>	KAHVEA	PIAGSMLLAA	
<i>Xenopus laevis</i>	MVKMPYGLH LWL	<b>P</b>	KAHVEA	PIAGSMVLAA	
<i>Salmo salar</i>	LVKMPVYGVH LWL	<b>P</b>	KAHVEA	PIAGSMILAA	
<i>Drosophila melanogaster</i>	LVKMPMFLVH LWL	<b>P</b>	KAHVEA	PVSGSMILAG	

### T14138C

<b>ND5 a.a. sequences</b>	590	600	601
<i>Homo sapiens</i>	GMIKLYFLSP FFFPLVLTLL	<b>L</b>	IT
<b>ColoLivM-5 (L601P)</b>	GMIKLYFLSP FFFPLVLTLL	<b>P</b>	IT
<i>Mus musculus</i>	GLIKLYFMSN FLINIILIII	<b>L</b>	YSINLE
<i>Bos taurus</i>	GLIKLYFLST FLITILISMI	<b>L</b>	FNPFHE
<i>Gallus gallus</i>	GLIKSYLGST FALTILTIL	<b>L</b>	IQK
<i>Xenopus laevis</i>	GLIKTYLTLT FLMTSAIIIT	<b>L</b>	F
<i>Salmo salar</i>	GMIKTYLTLT FFLSTALAVL	<b>L</b>	TLT
<i>Drosophila melanogaster</i>	NSLKIYLLW FVFWILILLI	<b>L</b>	LFL

**Supplementary Fig. S2.** Selected SNVs found in clinical samples that cause the substitution of evolutionarily highly conserved amino acids.