Additional material 1: SURF1 study data collection questionnaire

Name of hospital	
Speciality of managing consultant (Metabolic, Neurology, General Paediatric or other specify)	Metabolic ☐ Neurology☐ General Paediatric ☐ other specify☐

Patient demographics

Patient	
Date of birth	
Ethnicity	
Gender	
Is the patient alive or deceased?	
If deceased, please give age or date of death.	
If deceased, please give cause of death.	

Family history

Is there a history of consanguinity?	
If so, degree of relationship	
Does the patient have any affected siblings? Please give sex and ages of affected siblings.	
Pedigree	

Prenatal history:

Prenatal and birth history	**Details**
Problems noted during pregnancy of the affected child?	
Peri partum issues?	
Mode of delivery and gestational age at the time of birth.	
Birth weight and centile	
Birth length and centile	
Birth head circumference and centile	

Clinical Features

Clinical Diagnosis	**Tick as appropriate**
Leigh Syndrome	
Leukoencephalopathy	
Other (please specify)	

Initial symptoms and age at first presentation	

Subsequent symptoms and age of onset

Clinical feature	Yes/ No	If yes, age of onset	Other information
Poor feeding or vomiting?			
Evidence of poor growth?			Weight centile at age Height centile at age
Hypotonia or floppy?			

Clinical feature	Yes/ No	If yes, age of onset	Other information
Movement disorder (e.g. tremor, chorea etc)			Please specify type
Ataxia?			
Developmental delay?			Motor ☐ Speech ☐ Intellectual ☐ Global ☐
Developmental regression?			Any triggering factors?
Encephalopathy?			
Seizures?			Generalised tonic clonic ☐ Myoclonic ☐ Absence seizures ☐ Other ☐ Specify
Nystagmus?			Horizontal ☐ Vertical ☐ Rotatory ☐
Ptosis or ophthalmoplegia?			
Optic atrophy?			
Pigmentary retinopathy?			
Sensorineural hearing loss?			
Peripheral neuropathy?			
Hypertrichosis?			
Dermatological problems?			
Respiratory failure?			
Any other symptoms or signs not mentioned above?			
Age at definitive diagnosis?			
Number of PICU admissions			Cause for each admission

Other information (free text)

Is the patient in mainstream school? Please give details (special needs etc)
Does the patient require any specific aids? e.g. wheelchair. Please give age at which these were first required

Imaging and EEG findings: **if you have an electronic version of the report please copy and paste**

Investigation	Date	Result
MRI brain scan 1		
MRI brain scan 2 (if more than one scan)		
MRI brain scan 3 (if more than two scans)		
EEG findings		
Echocardiogram (cardiac) findings Cardiomyopathy? (If so, hypertrophic or dilated?)		
ECG abnormality (Conduction defect?)		
Nerve conduction studies/ EMG		

Treatment

Treatment	Yes/No	Details
Coenzyme Q_{10} (Ubiquinone)		

Other vitamins? Singly or in cocktail?		
Naso-gastric or PEG feeding (please give age of commencement)		

Investigations: (if you have an electronic version of the report please copy and paste or attach copy)

1. **Muscle biopsy**

Ragged red fibres	SDH-positive fibres	COX-negative fibres (if so, patchy or homogeneous)	Ragged blue fibres (on COX/SDH stain)	Excess lipid	Electron microscopy changes	Other muscle histological abnormalities

2. Respiratory chain enzyme activities: Please give reference ranges for each item.

Enzyme activity	In muscle	Ref range	In liver	Ref range	In fibroblasts	Ref range
Complex I						
Complex II+III						
Complex IV						
Complex V						

	muscle	white cell
Coenzyme Q_{10} level		

3. Other metabolic investigations. Please include interpretive comments (e.g. for organic acid results) provided by the lab and local reference ranges

Investigation	Date of investigation	Result (with units)	Reference range
Serum lactate			
Serum pyruvate			
Serum lactate/pyruvate ratio			
If serum lactate was done more than once please give range (e.g from 2.1 to 4 mmol/L)			
Metabolic acidosis? If yes, please give pH & HCO_3 below			
pH			
HCO_3			
Plasma amino acids (PAA) - Alanine - Other abnormalities in PAA			
Blood spot or plasma acylcarnitines			
Hypoglycaemia? If yes give result			
Ketosis?			
Urine organic acids			
CSF amino acids - Alanine - Other abnormalities			
CSF protein			
CSF lactate			
CSF pyruvate			
CSF lactate/pyruvate ratio			

CSF neurotransmitters			
Renal tubular function Urine retinol binding protein/creatinine RBP/Cr ratio			
Renal tubular function Urine N-acetylglucosaminidase NAG/Cr ratio			
Endocrine disturbance? Please specify			

Any other relevant information not indicated above

Additional table 1: Patient phenotypes and genotypes published in the literature

	Age of onset	Age of death	Clinical features	MRI	Blood lactate	CSF lactate	Histology	COX histo-chemistry	Muscle COX	Fibro-blast COX	Mutation allele 1*	Mutation allele 2*	Reference
1	NA	NA	Hypotonia, truncal ataxia, ophthalmoplegia, psychomotor regression, respiratory failure	NA	NA	NA	NA	NA	low	low	c.37ins17	c.37ins17	Tiranti et al 1998
2	NA	NA	Hypotonia, truncal ataxia, ophthalmoplegia, psychomotor regression, respiratory failure	NA	NA	NA	NA	NA	low	low	c.550delAG	c.516+2	Tiranti et al 1998
3	NA	NA	Hypotonia, truncal ataxia, ophthalmoplegia, psychomotor regression, respiratory failure	NA	NA	NA	NA	NA	low	low	c.868insT	c.868insT	Tiranti et al 1998
4	NA	NA	Hypotonia, truncal ataxia, ophthalmoplegia, psychomotor regression, respiratory failure	NA	NA	NA	NA	NA	low	low	c.312_321del 10insAT	c.312_321del 10insAT	Tiranti et al 1998
5	NA	NA	Hypotonia, truncal ataxia, ophthalmoplegia, psychomotor regression, respiratory failure	NA	NA	NA	NA	NA	low	low	c.845delCT	c.845delCT	Tiranti et al 1998
6	NA	NA	Hypotonia, truncal ataxia, ophthalmoplegia, psychomotor regression, respiratory failure	NA	NA	NA	NA	NA	low	low	c.845delCT	c.312_321del 10insAT	Tiranti et al 1998
7	NA	NA	Hypotonia, truncal ataxia, ophthalmoplegia, psychomotor regression, respiratory failure	NA	NA	NA	NA	NA	low	low	c.751C>T	c.751C>T	Tiranti et al 1998
8	NA	NA	Hypotonia, truncal ataxia, ophthalmoplegia, psychomotor regression, respiratory failure	NA	NA	NA	NA	NA	low	low	c.845delCT	c.845delCT	Tiranti et al 1998

9	NA	NA	Hypotonia, truncal ataxia, ophthalmoplegia, psychomotor regression, respiratory failure	NA	NA	NA	NA	NA	low	low	c.772delCC	c.772delCC	Tiranti et al 1998
10	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.751C>T	c.323+2T>C	Zhu et al 1998
11	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.845_846delCT	c.312_321del10insAT	Zhu et al 1998
12	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.868insT	c.868insT	Zhu et al 1998
13	16 months	3 years	Typical LS	NA	LS	NA	NA	NA	low	low	c.751C>T	c.751C>T	Tiranti et al 1999
14	12 months	3 years	Typical LS	NA	LS	NA	NA	NA	low	low	c.588insCTGC	c.74G>A	Tiranti et al 1999
15	11 months	4 years	Typical LS	NA	LS	NA	NA	NA	low	low	c.552delG	c.552delG	Tiranti et al 1999
16	12 months	4 years	Typical LS	NA	LS	NA	NA	NA	low	low	c.312del10,insAT	c.312del10,insAT	Tiranti et al 1999
17	12 months	4 years	Typical LS	NA	LS	NA	NA	NA	NA	low	c.312del10,insAT	c.845delCT	Tiranti et al 1999
18	7 months	6 years	Typical LS	NA	LS	NA	NA	NA	NA	low	c.37ins17	c.37ins17	Tiranti et al 1999
19	10 months	2 years	Typical LS	NA	LS	NA	NA	NA	NA	low	c.868insT	c.868insT	Tiranti et al 1999
20	6 months	alive at 8 years	Typical LS	NA	LS	NA	NA	NA	low	low	c.845delCT	c.845delCT	Tiranti et al 1999
21	9 months	died at 6 years	Typical LS	NA	LS	NA	NA	NA	low	low	c.552delG	c.552delG	Tiranti et al 1999
22	9 months	7 years	Typical LS	NA	LS	NA	NA	NA	low	low	c.312_321del10insAT (p.L105X)	c.822G>T	Tiranti et al 1999
23	13 months	3 years	Typical LS	NA	LS	NA	NA	NA	low	low	c.588insCTGC	c.588insCTGC	Tiranti et al 1999
24	5 months	alive 4 year	Typical LS	NA	LS	NA	NA	NA	low	NA	c.758del2bp	c.758del2bp	Tiranti et al 1999
25	16 months	3 years	Typical LS	NA	LS	NA	NA	NA	low	low	c.516+2T>G	c.552delG	Tiranti et al 1999
26	12 months	9 years	Typical LS	NA	LS	NA	NA	NA	low	low	c.239+1T>G	c.239+1T>G	Tiranti et al 1999

27	14 months	3 years	Typical LS	NA	LS	NA	NA	NA	low	low	c.312_321del 10insAT (p.L105X)	c.312_321del 10insAT (p.L105X)	Tiranti et al 1999
28	8 months	3 years	Typical LS	NA	LS	NA	NA	NA	low	NA	c.845delCT	c.845delCT	Tiranti et al 1999
29	12 months	8 years	Typical LS	NA	LS	NA	NA	NA	low	NA	c.845delCT	c.845delCT	Tiranti et al 1999
30	Died	14 years	Typical LS	NA	LS	NA	NA	NA	low	low	c.772_773del CC	c.772_773del CC	Tiranti et al 1999
31	10 months	alive at 18 months	Motor developmental delay, ophthalmoplegia, respiratory failure	Bilateral, symmetrical signal increases in basal ganglia, cerebellum dentate nucleus, and around aqueduct of midbrain	normal	high	Variation in fibre size	low	NA	NA	c.790delAG	c.820C>G	Teraoka et al1999
32	shortly after birth	6 years	Developmental delay, short stature, hypertrichosis, intention tremor, hypotonia	Bilateral and symmetric areas of lucencies in the brainstem and cerebellum	high	NA	Variation in fibre size	low	low	NA	c.258C>T	c.258C>T	Santoro et al 2000
33	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.312_321del 10insAT	c.587_588ins CAGG	Sue et al. 2000
34	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.845_846del CT	c.814delCT	Sue et al. 2000
35	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.845_846del CT	c.845_846del CT	Sue et al. 2000
36	2 years	alive at 7 years	Tremor, cerebellar ataxia, deafness, dystonia, ophthalmoplegia, encephalopathy	NA	NA	NA	NA	NA	NA	NA	G618 C, T751 C	c.766–3C>G	Poyau et al 2000
37	14 months	3 years	Hypotonia, abnormal involuntary movements, tremor, ataxia, deafness, partial Fanconi syndrome, severe encephalopathy, cardiomyopathy	NA	high	NA	NA	NA	NA	NA	c.702C>T	c.589ins CTGC	Poyau et al 2000

38	4 years	alive at 4 years	Short stature, psychomotor regression, muscular atrophy, hypotonia, encephalopathy	NA	NA	NA	Ragged red fibres	low	NA	NA	c.312_321del 10insAT	c.385G>A e	Poyau et al 2000
39	3 years	alive at 3 years	NA	NA	NA	NA	NA	NA	NA	NA	c.312_321del 10insAT	c.385G>A e	Poyau et al 2000
40	2 months		Vomiting , hypotonia, developmental delay, poor growth, nystagmus, tremors	High intensity in lenticular nucleus	high	NA	NA	low	NA	N|A	Homozygous insertion of one base in exon 9	Homozygous insertion of one base in exon	Savasta et al 2001
41	9 months	4 years	Poor growth, swallowing difficulties, hypotonia, trunk ataxia, nystagmus, optic atrophy, demyelinating peripheral neuropathy	Symmetric lesions of basal ganglia and brain stem	high	NA	NA	NA	low	NA	c.312_321del 10insAT	c.588+1delG	Pe´quignot et al 2001
42	NA	alive at 14 years	Psychomotor delay, ataxia, ophthalmoplegia, retinopathy, demyelinating neuropathy, recurrent vomiting attacks and regression	Brain stem, thalamus and cerebellar atrophy	high	NA	NA	NA	low	NA	c.312_321del 10insAT	c.737T>C	Pe´quignot et al 2001
43	12 months	2 years	Poor growth, trunk ataxia, dystonia, swallowing difficulties in swallowing, respiratory distress, optic atrophy, demyelinating neuropathy	Bilateral symmetrical lesions of the basal ganglia and the brain stem	high	NA	NA	NA	low	NA	c.240+1G >T	c.588+1G>A	Pe´quignot et al 2001
44	NA	18 months	Vomiting, developmental delay, hypotonia	NA	NA	NA	NA	NA	low	NA	c.516–2_516–1delAG	c.516–2_516–1delAG	Pe´quignot et al 2001
45	6 months	34 months	Poor growth, hypertrichosis, ophthalmoplegia, hypotonia, severe cerebellar disturbances	Symmetrical lesions of the basal ganglia	high	high	NA	NA	low	low	c.312_321del 10insAT	c.821del18	Williams et al 2001

46	birth	6 years	Hypotonia, muscle weakness, ataxia, dystonia, choreoathetosis, poor growth, hypertrichosis, hepatopathy	NA	high	high	NA	NA	low	NA	c.688C>T	c.820-821dup	Darin et al 2001
47	12 months	alive at 1 year	Hypotonia, muscle weakness, ataxia, dystonia, choeoathetoiss, poor growth,,	NA	high	high	NA	NA	low	NA	c.312_321del 10insAT	c.312_321del 10insAT	Darin et al 2001
48	5 months	alive at 5 months	Nystagmus, hypotonia, neuropathy, poor growth	NA	high	high	NA	NA	low	NA	c.688C>T	C.751+1G>A	Darin et al 2001
49	6 months	3 years	Sudden poor growth, vomiting, major hypertrichosis, ophthalmoplegia, hypotonia	CT scan was normal	high	NA	NA	NA	low	low	c.539G>A, p.G160E	c.603-1G>C	Von Kleist Retzow et al 2001
50	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.367_368del AG	c.367_368del AG	Ogawa et al 2002
51	12-15 months	alive at 15 months	Poor feeding, short stature, muscle weakness, movement disorder, liver involvement, hypertrichosis	Bilateral hyperintense lesions in putamen, the subcortical white matter, cerebral peduncles, pons, medulla oblongata, nucleus dentatus	NA	NA	NA	NA	low	NA	c.312_321del 10insAT	c.312_321del 10insAT	Moslemi et al 2003
52	5 months	alive at 5 months	Poor feeding, short stature, muscle weakness, movement disorder, nystagmus, external ophthalmoplegia	Hyperintense lesions on T2-weighted imaging in putamen, the cerebral peduncles, pons, and around the aqueductus cerebri.	NA	NA	NA	NA	low	NA	c.688C>T	tandem duplication (806–820) in exon 8,	Moslemi et al 2003
53	5 months	NA	Poor feeding, short stature, nystagmus	NA	NA	NA	NA	NA	low	NA	c.688C>T	C.751+1G>A	Moslemi et al 2003

54	NA	NA	Poor growth, progressive muscle hypotonia, hypertrichosis, developmental delay, amaurosis	Symmetrical basal ganglia lesions	NA	NA	NA	NA	NA	low	c.841delCT	c.841delCT	Pecina et al 2003
55	NA	NA	Poor growth, progressive muscle hypotonia, hypertrichosis, developmental delay, ophthalmoplegia	Symmetrical basal ganglia lesions	NA	NA	NA	NA	NA	low	c.312_321del 10insAT	c.821del18	Pecina et al 2003
56	NA	alive at 11 years	Poor growth, progressive muscle hypotonia, hypertrichosis, developmental delay, nystagmus	symmetrical basal ganglia lesions	NA	NA	NA	NA	NA	low	841delCT mutation	c.574C>T	Pecina et al 2003
57	14 months	22 months	Developmental delay, hypotonia, regression, peripheral neuropathy, respiratory failure	Brain MRI at 16 months: showed bilateral, symmetric lesions involving the medulla above, at, and below the pyramidal decussation and symmetrically the inferior cerebellar peduncles, substantia nigra, central tegmental tracts, and subthalamic nuclei	high	NA	NA	absent	low	NA	c.240+1G >T	c.531_534del AAAT	Rossi et al 2003

58	12 months	alive at 3 years	Poor growth, neurodevelopmental regression, frequent vomiting, hypertrichosis, hypotonia	Brain MRI: T2 prolongation involving the medulla above, at, and below the pyramidal decussation and extending to the cervical spinal cord, inferior cerebellar peduncles, dentate nuclei, substantia nigra, and subthalamic nuclei	high	NA	NA	absent	low	NA	c.566delG	mutation at splice-junction site of intron 4	Rossi et al 2003
59	1 st year	alive at 4 years	Poor growth, neurodevelopmental delay, palpebral ptosis, impaired consciousness, facial dysmorphism, hirsutism, nystagmus, hypotonia, respiratory abnormalities.	Brain MR imaging was performed at age 3 years: medulla, inferior cerebellar peduncles, dentate nuclei, midbrain, substantia nigra, central tegmental tract, interpeduncular nucleus, pallido-cortical–nigro-cortical tracts. subthalamic nuclei, putamina	high	NA	NA	absent	low	NA	c.772_773del CC	c.772_773del CC	Rossi et al 2003
60	NA	NA	Poor growth, progressive muscle hypotonia, hypertrichosis, developmental delay, ophthalmoplegia	Symmetrical basal ganglia lesions	NA	NA	NA	NA	NA	low	c.688C>T,	c.688C>T	Pecina et al 2003
61	4 months	alive at 8 years	Poor growth, developmental delay, ataxia, nystagmus, tremors, dysphagia, respiratory failure	NA	NA	NA	NA	NA	low	NA	c.312_321del 10insAT	c.572_573ins CCCT	Salviati et al 2004

62	NA	NA	Poor feeding, hypotonia, poor growth, developmental delay, respiratory abnormalities	Neuroradiological changes of Leigh syndrome on neuroimaging	high	NA	NA	NA	NA	NA	c.312_321del 10insAT		Head et al 2004
63	NA	NA	Poor feeding, hypotonia, poor growth, developmental delay, respiratory abnormalities	Neuroradiological changes of Leigh syndrome on neuroimaging	high	NA	NA	NA	NA	NA	c.312_321del 10insAT		Head et al 2004
64	NA	NA	Poor feeding, hypotonia, poor growth, developmental delay, respiratory abnormalities	Evidence only of cerebral atrophy, particularly affecting the frontal and parietal cortex	normal	high	NA	NA	NA	NA			Head et al 2004
65	4 months	alive at 42 months	Poor growth, psychomotor developmental delay, nystagmus, ataxia tremor, dysphagia, apnoea	First MRI brain at 39 months normal. Second study at 8 years: diffuse supratentorial atrophy, severe cerebellar hemisphere atrophy, and cystic-like changes inferior to pontine brainstem. White matter signal intensity in supratentorial region normal and basal ganglia also appeared normal	normal	NA	NA	NA	NA	NA	c.312_321del 10insAT	c.572_573ins CCCT;	Salviati et al 2004
66	6 months	alive at 11 months	Persistent vomiting, poor growth, developmental regression, cardiomyopathy, respiratory failure, distal tubular acidosis	8 months: symmetric bilateral signal abnormalities throughout brain stem, cerebellum, and diencephalon and a remote posterior inferior cerebellar artery infarction	high	high	NA	low	NA	NA	c.312_321del 10insAT	c.688C>T	Tay et al 2005

67	10 months	2 years	Developmental regression, hypotonia, nystagmus, optic atrophy, bilateral Babinski reflexes, respiratory abnormalities, proximal tubular acidosis	Right and left putamen globus pallidus showed oedema	high	NA	Type 1 fibre atrophy	low	low	low	c.834G>A	c.834G>A	Tay et al 2005
68	3 months	2 years	Loss of head control, poor growth, truncal ataxia, hypertrichosis, respiratory abnormalities	Midbrain tegmentum, brain stem, dentate nucleus.	high	NA	NA	low	low	low	c.834G>A	c.834G>A	Tay et al 2005
69	10 months	alive at 10 months	Vomiting, regression, motor delay, tubular acidosis	Bilateral abnormal signals in the putamen and caudate nuclei	normal	high	Increased lipid and ragged red fibres	low	low	low	c.312_321del 10insAT	c.820–824dupTACAT	Tay et al 2005
70	2 months	2 year and 7 months	poor growth, progressive developmental delay, muscle weakness, hypertrichosis, squint	2½ years: symmetric bilateral hyperintense lesions at T2, dentate nuclei, mesencephalic nuclei, periaqueductal parenchyma, and medulla oblongata	high	NA	NA	NA	low	low	c.312_321del 10insAT	c.845delCT	Østergaard et al 2005
71	6 weeks		Psychomotor development delay, hypotonia, ataxia, dystonia ataxia, hypertrichosis, gastrostomy feeding	CT scan: symmetrical lesions in basal ganglia	NA	NA	NA	NA	low	low	c.312_321del 10insAT	c.688C>T	Østergaard et al 2005
72	10 months	9 years	Psychomotor developmental delay, poor growth, ophthalmoplegia, ataxia, spasticity, hypertrichosis	NA	NA	NA	NA	NA	low	low	c.312_321del 10insAT	c.312_321del TCTGCCAGCCinsAT	Østergaard et al 2005
73	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.240+1G>C,	NA	Yang et al 2006
74	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.574C>G,	NA	Yang et al 2006
75	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.622delA	NA	Yang et al 2006

76	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.653-654delCT	NA	Yang et al 2006
77	23 months	alive at 23 months	regression, poor growth, hypotonia	2 years: hypointense lesion of subthalamic nuclei, brainstem involvement; second MRI at 3 years: mild cerebellar and marked cerebral atrophy, diffuse involvement of substantia nigra, hyperintense lesion of central tegmental tract, and extensive brainstem involvement	NA	high	NA	NA	NA	NA	c.244C>T	c.244C>T	Yüksel et al 2006
78	13 months	alive at 3 years	Psychomotor regression, developmental delay, failure to thrive, neurodevelopmental regression, generalized hypotonia, respiratory problems, and absent deep facial dysmorphism including frontal bossing, brachycephaly, hypertrichosis	Heavy brainstem and subthalamic nuclei involvement without lesions in basal ganglia; second MRI at 2 years indicated heavy brainstem and subthalamic nuclei involvement without lesions in basal ganglia	NA	high	NA	NA	low	low	c.530T>G	c.530T>G	Yüksel et al 2006
79	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.845-846delCT	c.845-846delCT	Bohm et al 2006
80	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.845-846delCT	c.845-846delCT	Bohm et al 2006
81	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.845-846delCT	c.312_321del 10insAT	Bohm et al 2006
82	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.845-846delCT	c.574C>T	Bohm et al 2006
83	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.845_846del CT	c.756delCA	Bohm et al 2006
84	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.845_846del CT	c.704T>C	Bohm et al 2006

85	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.845_846del CT	c.821A>G	Bohm et al 2006
86	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.821-838del18	c.821-838del18	Bohm et al 2006,
87	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.312_321del 10insAT	c.821-838del18	Bohm et al 2006
88	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.312_321del 10insAT	c.312_321del 10insAT	Bohm et al 2006
89	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.688C>T	c.688C>T	Bohm et al 2006
90	2 years	6 years	ataxia, hypotonia, nystagmus	typical of leigh	high	high	NA	NA	low	low	c.370G>A	c.370G>A	Coenen et al 2006
91	NA	NA	Leigh	NA	NA	NA	NA	NA	NA	low	C.244C>T	c.312_321del 10insAT	Coenen et al 2006
92	NA	NA	Leigh	NA	NA	NA	NA	NA	NA	low	c.239G>A	c.312_321del 10insAT	Coenen et al 2006
93	NA	NA	Leigh	NA	NA	NA	NA	NA	NA	low	c.312_321del 10insAT	c.312_321del 10insAT	Coenen et al 2006
94	12 months	5 years	Poor growth, developmental delay, microcephaly. hypertrichosis, synophrys, hypotonia, peripheral neuropathy and truncal ataxia	Lesions in caudal parts of brain stem resulting in distension of medulla oblongata and lesions in central myelin of cerebellum	high	high	normal	normal	low	low	c.867G>A	c.867G>A	Van Riesan et al 2008
95	4 months	alive at 4 months	Motor regression, hypotonia, hypertrichosis, bulbar symptoms	NA	high	NA	NA	NA	low	NA	c.841delCT	NA	Pronicki et al 2008
96	12 months	alive at 12 months	Trembling, ataxia gait, myoclonic jerks, ophthalmoplegia	Hyperintense signals at lenticular nuclei	NA	NA	NA	NA	low	NA	c.841delCT	NA	Pronicki et al 2008
97	30 months	alive at 30 months	Dystonic movements, poor growth	Symmetric hyperintense signals at lenticular and caudate nuclei, medulla oblongata putamen, globi pallidi	NA	NA	NA	NA	low	NA	c.841delCT	NA	Pronicki et al 2008

98	5 months	alive at 5 months	Poor growth, hypotonia, nystagmus, trembling, hypertrichosis, respiratory failure	NA	NA	NA	NA	NA	low	NA	c.841delCT	C.841delCT	Pronicki et al 2008
99	12 months	4 years	Poor growth, vomiting, respiratory abnormalities	Symmetric hypodense changes in basal ganglia	NA	NA	NA	NA	NA	NA	c.841delCT	C.841delCT	Pronicki et al 2008
100	16 months	alive at 16 months	Speech difficulties, hypotonia, nystagmus, developmental regression.	NA	NA	NA	NA	NA	low	NA	c.841delCT	NA	Pronicki et al 2008
101	2 years	Alive at 2 years	Difficulty in walking and speaking, poor growth, ophthalmoplegia, hypertrichosis, respiratory abnormalities	NA	NA	NA	NA	NA	low	NA	c.841delCT	C.841delCT	Pronicki et al 2008
102	12 months	alive at 12 months	Poor growth, hypotonia, hypertrichosis, respiratory abnormalities	NA	NA	NA	NA	NA	NA	NA	c.841delCT	C.841delCT	Pronicki et al 2008
103	14 months	30 months	14 months: regression of motor skills, poor growth, hypertrichosis, tremor, ophthalmoplegia, respiratory abnormalities	NA	NA	NA	NA	NA	low	NA	c.841delCT	C.841delCT	Pronicki et al 2008
104	3 months	alive at 3 months	Poor growth, hypotonia, hypertrichosis	CT: hypodensic areas in both cerebellar hemispheres and caudate nuclei	NA	NA	NA	NA	low	NA	c.841delCT	C.841delCT	Pronicki et al 2008
105	16 months	10 years	Nystagmus, speech and walking difficulties	NA	NA	NA	NA	NA	low	NA	c.841delCT	NA	Pronicki et al 2008
106	9 months	alive at 9 months	Hypotonia, hypotonia, poor growth, vomiting, tremor	NA	NA	NA	NA	NA	NA	NA	c.841delCT	C.841delCT	Pronicki et al 2008
107	19 months	alive at 19 months	Tremor, ophthalmoplegia, dystonia, respiratory failure	CT: Symmetric hypodense areas of basal ganglia	NA	NA	NA	NA	low	NA	c.841delCT	C.841delCT	Pronicki et al 2008

108	12 months	alive at 12 months	Hypotonia, respiratory abnormalities, ophthalmoplegia, hypertrichosis	MRI at 2.5 years: symmetric hyperintense signals in basal ganglia	NA	NA	NA	NA	low	NA	c.841delCT	NA	Pronicki et al 2008
109	4 months	alive at 4 months	Motor regression, poor growth, hypotonia, tremor, hypertrichosis, ophthalmoplegia	NA	high	NA	NA	NA	low	NA	c.841delCT	C.841delCT	Pronicki et al 2008
110	2 months	alive at 2 months	Hypotonia, vomiting, respiratory abnormalities, ophthalmoplegia, ptosis, hypertrichosis	MRI at 4 years: symmetric hyperintense signals in basal ganglia, brain atrophy	NA	NA	NA	NA	low	NA	c.841delCT	C.841delCT	Pronicki et al 2008
111	7 months	alive at 7 months	Poor growth, vomiting, hypotonia, hypertrichosis, ophthalmoplegia	NA	NA	NA	NA	NA	low	NA	c.841delCT	C.841delCT	Pronicki et al 2008
112	14 months	alive at14 months	Motor regression, trembling, hypertrichosis, hypotonia	MRI: symmetric hyperintense signals in basal ganglia	NA	NA	NA	NA	low	NA	c.841delCT	C.841delCT	Pronicki et al 2008
113	7 months	alive at 7 months	Motor regression, respiratory abnormalities, vomiting	MRI: symmetric hyperintense signals in basal ganglia	high	NA	NA	NA	low	NA	c.841delCT	C.841delCT	Pronicki et al 2008
114	1st year	alive at 12 months	Poor growth, vomiting, tremor, respiratory abnormalities	NA	high	NA	NA	NA	low	NA	c.841delCT	NA	Pronicki et al 2008
115	6 months	alive at 6 months	Poor growth, hypotonia, respiratory abnormalities	MRI: symmetric hyperintense signals at lenticular nuclei, putamen, crura cerebri, substantia nigra, cerebellum periventricular areas,medulla oblongata	high	NA	NA	NA	low	NA	c.841delCT	C.841delCT	Pronicki et al 2008

116	2 years	alive at 8 years	Psychomotor development delay, hypotonia, ataxia, converging squint. Hypertrichosis	NA			Atrophic vacuolated fibres with numerous oil red O positive lipid droplets	low	NA	NA	NA	NA	Angelini et al 2009
117	16 months	13 years 8 months	Hypotonia, speech and walking difficulties, nystagmus	NA	high	high	NA	NA	NA	NA	c.821A>G	c.845delCT	Piekutowska-Abramczuk et al 2009
118	20 months	7 years 5 months	Progressive muscle atrophy, speech and walking disturbances, nystagmus	NA	NA	high	NA	NA	NA	NA	c.821A>G	c.845delCT	Piekutowska-Abramczuk et al 2009
119	36 months	alive at 60 month	Walking and speech difficulties, failure to thrive	NA	NA	NA	NA	NA	NA	NA	c.821A>G	c.845delCT	Piekutowska-Abramczuk et al 2009
120	12 months	6 years and 7 month	Hypotonia, psychomotor retardation, muscle weakness	NA	NA	NA	NA	NA	NA	NA	c.821A>G, p.Tyr274Cys	c.845delCT	Piekutowska-Abramczuk et al 2009
121	24 months	4 years and 5 months	Walking difficulties, hypotonia, nystagmus	NA	NA	NA	NA	NA	NA	NA	c.821A>G	c.845delCT	Piekutowska-Abramczuk et al 2009
122	24 months	alive 24 months	Walking difficulties, nystagmus	NA	NA	NA	NA	NA	NA	NA	c.821A>G	c.845delCT	Piekutowska-Abramczuk et al 2009
123	24 months	20 years and 10 months	Walking difficulties, failure to thrive, echolalia	Lentiform nuclei right globus palladus, ventral medulla, enlarged ventricles, especially frontal horns	NA	NA	NA	NA	low	NA	c.704T>C	c.845delCT	Piekutowska-Abramczuk et al 2009
124	42 months	alive at 60 months	Hypotonia, mild psychomotor retardation	NA	NA	NA	NA	NA	low	low	c.574C>T	c.845delCT	Piekutowska-Abramczuk et al 2009

125	6 months	alive at 18 months	Jerky head movements, infantile spasm, developmental delay and regression	Moderate brain atrophy. No abnormal signal was detected in the white matter or in the nuclei	NA	NA	NA	NA	NA	NA	c.604G>C	c.604G>C	Xie et al 2009
126	6 months	alive at 1 year	Poor feeding, hypotonia, developmental regression	Moderate brain atrophy. No abnormal signal was detected in the white matter or in the nuclei	NA	NA	NA	NA	NA	NA	c.604G>C	c.604G>C	Xie et al 2009
127	3 years	5 years	Hypotonia and ataxia	Bilateral putamen subthalamic nuclei substantia nigra, periaqueductal area, bilateral superior cerebellar peduncle, central tegmental tract, and dentate nuclei, the inferior olivary nuclei, dorsolateral medulla	NA	NA	NA	NA	NA	NA	c.604G>C	c.604G>C	Xie et al 2009
128	3 years	alive at 3 years	Ophthalmoplegia	Subthalamic nuclei, medial thalamic nuclei, midbrain, substantia nigra and central tegmental tract involved at superior colliculus level; tegmentum in pons and medulla	NA	NA	NA	NA	NA	NA	c.604G>C	c.604G>C	Xie et al 2009
129	3 years	alive at 12 years	Motor developmental delay, ophthalmoplegia, dysarthria	Moderate cerebral atrophy and severe cerebellar atrophy, hyperintense bilateral internal capsule and centrum semiovale	NA	NA	NA	NA	NA	NA	c.604G>C	c.604G>C	Xie et al 2009

130	1 year	alive at 8 years	Motor impairment and speech delay	Bilateral basal ganglia, subthalamic nuclei, and brain stem, centrum semiovale was abnormal	NA	NA	NA	NA	NA	NA	c.604G>C	c.604G>C	Xie et al 2009
131	1 year	alive at 12 years	Psychomotor delay, dysarthria, hypotonia, ataxia	NA	NA	NA	NA	NA	NA	NA	604G>C	604G>C	Xie et al 2009
132	1 year	alive at 8 years	Psychomotor delay, dysarthria, hypotonia, ataxia	NA	NA	NA	NA	NA	NA	NA	604G>C	604G>C	Xie et al 2009
133	14 months	22 months	Developmental delay, hypotonia, poor growth, neurodevelopmental regression	Substantia nigra and subthalamic nucleus	high	NA	High lipid	low	low	low	c.240 +1G > T	C534delAAAT	Bruno et al 2009
134	13 months		Partial seizures, ataxia, nystagmus, right optic atrophy, hypotonia	Cerebellar hypodensities in white matter and dentate nuclei	high	NA	NA	NA	NA	NA	NA	NA	Timothy et al 2009
135	NA	NA	Poor growth, ataxia, hypertrichosis	Basal ganglia	high	NA	NA	NA	NA	NA	c.312_321del 10insAT	c.312_321del 10insAT	Lee et al 2012
136	NA	NA	Poor growth, myopathy, hypertrichosis	Basal ganglia	high	NA	NA	NA	NA	NA	c.312_321del 10insAT	c.312_321del 10insAT	Lee et al 2012
137	NA	NA	Poor growth, seizure	Basal ganglia	high	NA	NA	NA	NA	NA	c.240+1G>T	c.516-2A>G	Lee et al 2012
138	NA	NA	Poor growth	Basal ganglia	high	NA	NA	NA	NA	NA	c.312_321del 10insAT (p.L105X)	c.312_321del 10insAT (p.L105X)	Lee et al 2012
139	NA	NA	Nystagmus	Subthalamic nuclei, medulla, tegmentum	high	NA	NA	low	low	NA	c.845_846del CT	c.269T>C	Lee et al 2012
140	NA	NA	Short stature, poor growth, ataxia, ophthalmoplegia, sensorineural hearing loss, peripheral neuropathy	Basal ganglia	normal	NA	NA	NA	NA	NA	c.653_654del CT	c.807_810del 4ins9	Lee et al 2012

141	NA	NA	Seizures, ptosis, muscle weakness, hypotonia, dysmorphism	Leukodystrophy	high	NA	NA	NA	NA	NA	c.169delG	c.530T>G	Lee et al 2012
142	NA	NA	Poor growth, hypotonia, microcephaly	Leukodystrophy	normal	NA	NA	NA	NA	low	c.324-11T>G	c.324-11T>G	Lee et al 2012
143	NA	Alive at 3.5 years	Spastic diparesis, swallowing difficulty, ataxia, seizure, hypertrichosis	Basal ganglia	high	NA	NA	NA	NA	low	c.555_556delGA	c.769G>A	Lee et al 2012
144	NA	NA	Poor growth	Leukodystrophy	high	NA	NA	NA	NA	low	c.555_556delGA	c.574_575insCTGC	Lee et al 2012
145	NA	NA	NA	NA	NA	NA	NA	NA	NA	low	c.312_321del10insAT	c.574_575insCTGC	Lee et al 2012
146	NA	Died at 4.5 years	Hypotonia, ataxia, ophthalmoplegia, nystagmus	Basal ganglia, cerebellar and medulla	high	NA	NA	NA	NA	NA	c.574_575insCTGC	c.55-1G>A	Lee et al 2012
147	NA	Alive at 6 years	Poor growth, hypotonia, muscle weakness, ataxia, swallowing difficulties, VI nerve palsy, hypertrichosis	Basal ganglia	high	NA	NA	NA	NA	NA	c.312_321del10insAT	c.614G>A	Lee et al 2012
148	NA	Alive at 4 years	Poor growth, hypotonia, muscle weakness, swallowing difficulties, cardiovascular malformations, Down syndrome	Basal ganglia, midbrain	high	NA	NA	NA	NA	NA	c.312_321del10insAT	c.614G>A	Lee et al 2012
149	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	c.833+1G>A	c.833+1G>A	Lee et al 2012
150	NA	Alive at 4 years	Poor growth, hypotonia, ataxia, apnoea	Basal ganglia	high	NA	NA	NA	NA	NA	c.183_186delTCTT	c.312_321del10insAT	Lee et al 2012
151	NA	Died at 3.5 years	Poor growth, hypotonia, ataxia, myoclonic jerks, extrapyramidal movements	Basal ganglia, periaqueductal grey matter	high	NA	NA	NA	NA	NA	c.106+1G>C	c.106+1G>C	Lee et al 2012
152	NA	Alive at 3 years	Poor growth, hypotonia, ataxia, dystonia	Cerebellum, brainstem, and basal ganglia	high	NA	NA	NA	NA	NA	c.845_846delCT	c.107-2A>G	Lee et al 2012

153	NA	Alive at 5 years	Hypotonia, ataxia, nystagmus	Brainstem, cerebellum, basal ganglia, and right occipital white matter lesions	high	NA	NA	NA	NA	NA	c.472_473delAG	c.845delCT	Lee et al 2012
154	NA	Alive, at 2 years	Poor growth, hypotonia, muscle weakness	Basal ganglia, leukodystrophy	high	NA	NA	NA	NA	NA	c.312_321del10insAT (p.L105X)	c.845_846delCT (p.S282CfsX9)	Lee et al 2012
155	NA	Alive, at 3 years	Poor growth, hypotonia, chorea, cortical visual impairment, microcephaly, myoclonic epilepsy, gastro-oesphageal reflux,	Generalized volume loss and hypomyelination	NA	NA	NA	NA	low	NA	c.167C>G (p.A56G)	c.751+6T>C	Lee et al 2012
156	NA	NA	Developmental arrest, facial dysmorphism, hypertrichosis, Mild opthalmoplegia ptosis, mild hypotonia, truncal ataxia	Hyperintensity of the bilateral putamen, subthalamic nucleus, red nucleus and brain stem	high	NA	NA	NA	NA	NA	c.49+1 G>T	c.752_753del	Tanigawa 2012
157	19 months	alive at 8 years		Bilateral cerebral hemispheres globally atrophic, hyperintensity of bilateral optic radiation, putamen, basal ganglia including subthalamic nucleus, and globus pallidus.	NA	high	NA	NA	NA	low	c.743 C>A, p.Ala248Asp	c.743 C>A, p.Ala248Asp	Tanigawa 2012

*Mutation data is reported using the nomenclature used in the original papers; NA data not available

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