**Supplementary table 2:** Review of the literature

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Variant** | **No. of**  **reported**  **individuals** | **range of heteroplasmy**  **in patients**  **(%)** | **range of heteroplasmy**  **in asymptomatic carrier (%)** | **AAO**  **≤ 1 year**  **(No.**  **patients)** | **AAO**  **1-11 years**  **(No. patients)** | **AAO**  **12-17 years**  **(No. patients)** | **AAO**  **≥ 18**  **years**  **(No. patients)** | **Leigh syndrome**  **(No. patients)** | **NARP syndrome**  **(No. patients** | **CAA**  **(No. patients)** | **NP**  **(No. patients)** | **Other** |
| **m.8528T>C** | 5 | 88-98 |  | 5 |  |  |  |  |  |  |  | IC, LVNC (5) |
| **m.8609\_8610insC** | 1 | n.a. |  | 1 |  |  |  |  |  | 1 |  | Epilepsy (1) |
| **m.8611insC** | 1 | 60-80 |  | 1 |  |  |  |  |  | 1 |  | Encephalomyopathy (1) |
| **m.8618-8619insT** | 1 | 85 |  |  |  |  | 1 |  | 1 |  |  |  |
| **m.8668T>C** | 1 | 99 |  |  |  |  | 1 |  |  |  |  | LHON (1) |
| **m.8701A>G** | 11 | n.a. |  |  |  |  | 7; n.a. (4) |  |  |  |  | MIH and dilated CM (7), LHON (2) |
| **m.8719G>A** | 1 | het |  |  |  |  | n.a. |  |  | 1 |  | suspected MD (1) |
| **m.8836A>G** | 1 | 100 |  |  | 1 |  |  |  |  |  |  | LHON-like (1) |
| **m.8839G>C** | 1 | 21-88 |  |  |  |  | 1 |  | 1 |  |  |  |
| **m.8851T>C** | 4 | 87-100 |  |  | 3 |  | n.a. (1) |  |  | 1 |  | BSN (3), suspected MD (1) |
| **m.8860G>C** | 3 | n.a. |  |  |  |  | n.a. (3) |  |  |  |  | LHON (3) |
| **m.8950G>A** | 1 | 100 |  |  |  |  | n.a. (1) | 1 |  |  |  |  |
| **m.8969G>A** | 6 | 79-100 |  | 4 | 2 |  |  |  |  |  |  | MLASA (1), LA (2), suspected MD (2) |
| **m.8989G>C** | 1 | 33-94 |  |  |  |  | 1 |  | 1 |  |  |  |
| **m.8993T>C** | 75 | 64-100; n.a. (25) | 13-96 | 13 | 17 | 1 | 9; n.a. (35) | 40 | 5 | 20 | 4 | MR (7), DD (5), gait disturbance (1), RP (2), febrile seizure, followed by lasting vegetative state (1), seizures (3), hearing disturbances (2), hypotonia (7), cerebellar dysarthria (2), MMR (1), muscle weakness (8), MD in children with PIND (1), suspected MD (9) |
| **m.8993T>G** | 225 | 44-100 | 6-77 | 72; n.a. (18) | 30; n.a. (5) | 4 | 17; n.a. (79) | 87 | 39 | 18 | 14 | RP (21), muscle weakness (5), MR (28), NARP without NP (2), CM (2), seizures (17), hypotonia (16), DD (23), optic atrophy (2), features mimicking KSS (1), CM (2), SUD (2), severe infantile LA and encephalomyopathy (3), infantile spasms (6), cognitive impairment (7); migraine (4); retinal degeneration (7), cerebral palsy (1), BSNHL (4), suspected MD (32), MD in children with PIND (11) |
| **m.9011C>T** | 1 | 100 |  |  |  |  | 1 |  |  |  |  | LHON (1) |
| **m.9016A>G** | 3 | 100 |  |  |  |  | 2; n.a. (1) |  |  |  |  | LHON (3) |
| **m.9025G>A** | 3 | 100 | 100 | 1 |  |  |  | 1 |  |  |  |  |
| **m.9029A>G** | 1 | 100 | 85-95 |  |  |  | 1 |  |  |  |  | LHON-like (1) |
| **m.9032T>C** | 1 | 70-96 | 42-73 | 1 |  |  |  |  | 1 |  |  |  |
| **m.9035T>C** | 22 | 90-100; n.a. (2) |  |  | 5 |  | 16; n.a. (1) |  |  | 20 |  | suspected MD (2) |
| **m.9101T>C** | 1 | 100 |  |  |  |  | 1 |  |  |  |  | LHON (1) |
| **m.9127delAT** | 1 | het/10-82 |  |  |  |  | 1 |  | 1 |  |  |  |
| **m.9134A>G** | 1 | 90-95 |  | 1 |  |  |  |  |  |  |  | CM, hypotonia, LA |
| **m.9139G>A** | 2 | n.a. |  |  |  |  | 2 |  |  |  |  | LHON (2) |
| **m.9176T>G** | 5 | 100 | het-100 | 1; n.a. (4) |  |  |  | 4 |  | 1 |  | poor feeding, neurological symptoms (1); |
| **m.9176T>C** | 44 | 90-100; n.a. (7) | 5-100 | 11 | 10; n.a. (2) | 3 | 13; n.a. (5) | 21 |  | 17 | 5 | suspected MD (3); episodic weakness (1); ptosis (1); MD in children with PIND (2); BSN; resembling LS (2); SUD (1); RP (1); Seizures (1); CMT (3); DD and MR (2); BSNHL (1); optic atrophy (1); reduced vibration sense (5); spastic paraplegia (4); |
| **m.9185T>C** | 73 | 78-100 | 17-100 |  | 14; n.a. (4) | 2 | 39; n.a. (14) | 9 | 4 | 24 | 24 | MD in children with PIND (1), WPW (1), seizures and cardiac arrhythmia (1), ptosis (2), periodic paralysis (3), diplopia (3), CMT (22); late-onset SNHL (1), motor weakness (16), suspected MD (4 families), cognitive impairment and muscle weakness (2), epilepsy (1), severe psychomotor DD and poor balance (1), episodic weakness (2); Leigh-like syndrome (1) |
| **m.9191T>C** | 1 | 90-94 |  |  | 1 |  |  | 1 |  |  |  | CM (1) |
| **m.9203\_9204delAT** | 1 | het |  |  |  |  | n.a. (1) |  |  |  |  | suspected MD (1) |
| **m.9204\_9205delTA** | 1 | 100 |  |  |  |  | n.a. (1) |  |  |  |  | severe MMR (1) |
| **m.9205\_9206delAT** | 3 | 70-99 |  | 1 | n.a. (2) |  |  |  |  |  |  | encephalopathy and seizures (1), LA (2), PDR (1) |

Abbrevations: AAO= Age at onset; BSN= bilateral strial necrosis; BSNHL= bilateral sensorineural hearing loss; CAA= Cerebellar ataxia; CM= cardiomyopathy; CMT= Charcot-Marie-Tooth disease; DD= developmental delay; het= heteroplasmy; IC= infantile cardiomyopathy; KSS= Kearns Sayre Syndrome; LA= lactic acidosis; LHON= Leber hereditary optic neuropathy; LVNC= left ventricular noncompaction; LS= Leigh Syndrome; MD= mitochondrial disorder; MIH= maternal inherited hypertension; MLASA= mitochondrial myopathy, lactic acidosis and sideroblastic anemia; MMR= motor and mental retardation; n.a.= not available; NARP= neuropathy, ataxia, retinitis pigmentosa; No.= Number; NP= neuropathy; PDR= psychomotor developmental retardation; PIND= progressive intellectual and neurological deterioration; RP= retinitis pigmentosa; SUD= sudden unexpected death; SNHL= sensorineural hearing loss; WPW= Wolff-Parkinson-White syndrome