**S5 Table.** Mitogenome sequences carrying the m.14258G>A/*MT-ND6*, p.P139L in common databases (a total of 31,787 mitogenomes). The Family 2 proband is also included.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Genbank-HGDP-1000 GP ID** | **HmtDB Genome Identifier** | **Haplo-group** | **Private Variants** | **Haplogroup Diagnostic Missense Variants** | **Number of Mutational Events****m.14258G>A** | **Phenotype** |
| **Synonymous** | **Non-Coding (for protein)** | **Missense** |
| MF039863 | Family 2 proband | H5b | m.10248T>C/MT-ND3 | *16309A>C/MT-HV1* | m.9966G>A*/MT-CO3* (V254I), m.10680G>A/*MT-ND4L* (A71T), m.12033A>G/*MT-ND4* (N425S), 14258G>A/*MT-ND6* (P139L)e |  | 1 | LHON |
|  | PA\_EU\_XX\_0017 | H5b | 8251G>A/*MT-CO2* | 16309A>G/*MT-HV1* | 9966G>A/*MT-CO3* (V254I)12033A>G/*MT-ND4* (N425S)14258G>A/*MT-ND6* (P139L)e |  | Glioblastoma |
| HG00589 | AS\_CN\_0419 | F1a1 | 8697G>A/*MT-ATP6* | 203G>C/*MT-HV2*1709G>A/*MT-RNR2*16399A>G/*MT-HV1* | 14258G>A/*MT-ND6* (P139L) | 9053G>A/*MT-ATP6* (S176N)10609 T>C/*MT-ND4L* (M47T)12406 G>A/*MT-ND5* (V24I)13759 G>A/*MT-ND5* (A475T)13928 G>C/*MT-ND5* (S531T) | 1 | Normal |
| EF657644 | EU\_XX\_0538 | H1q3a | 5237A>G/*MT-ND2* | 1009T>C/*MT-RNR1* | 9948G>A/*MT-CO3* (V248I) | 14258G>A/*MT-ND6* (P139L) | 1 | Normal |
| JX153975 | EU\_DK\_0876 | H1q3a |  |  | 3511A>G/*MT-ND1* (T69A) | 14258G>A/*MT-ND6* (P139L) | Normal |
| KF161678 | EU\_DK\_1085 | H1q3a |  |  | 3511A>G/*MT-ND1* (T69A) | 14258G>A/*MT-ND6* (P139L) | Normal |
| KF162479 | PA\_EU\_DK\_0471 | H1q3a |  |  | 3511A>G/*MT-ND1* (T69A) | 14258G>A/*MT-ND6* (P139L) | Diabetes |
| KM252740 | XX\_XX\_5717 | H1q3a | 11266C>T/*MT-ND4* |  | 4084G>A/*MT-ND1* (V260D) | 14258G>A/*MT-ND6* (P139L) | Normal |
|  | PA\_EU\_XX\_0019 | H1q3a |  |  |  | 14258G>A/*MT-ND6* (P139L) | Glioblastoma |
| NA20811 | EU\_IT\_0707 | H1q3a |  |  |  | 14258G>A/*MT-ND6* (P139L) | Normal |
| KP340158 | n.a. | HV2a2b | 6563C>T/*MT-CO1* |  | 14258G>A/*MT-ND6* (P139L) |  | 1 | n.a. |
| KP340159 | n.a. | HV2a2b | 6563C>T/ *MT-CO1* |  | 14258G>A/*MT-ND6* (P139L) |  | n.a. |
| KC878720 | EU\_IT\_0585 | K1a | 6137T>C/ *MT-CO1*6329C>T/ *MT-CO1*8994G>A/*MT-ATP6*11038A>G/*MT-ND4*15253A>G/*MT-CYB* |  | 14258G>A/*MT-ND6* (P139L)14582A>G/*MT-ND6* (V31A) | 9055G>A/*MT-ATP6* (A177T)14798T>C/*MT-CYB* (F18L) | 1 | Normal |
| KC533510 | PA\_AF\_SF\_0059 | L0d2a1 | 10771A>G/*MT-ND4* |  | 5460G>A/*MT-ND2* (A331T)13508C>T/*MT-ND5* (S391F)14258G>A/*MT-ND6* (P139L) | 4025C>T/*MT-ND1* (T240M)4225A>G/*MT-ND1* (M307V)4232T>C/*MT-ND1* (I309T)5442T>C/*MT-ND2* (F325L) | 1 | Pediatric patients |
| NA18868 | AF\_NG\_0078 | L2a1c1a1 |  | 2242T>C/*MT-RNR2* | 8584G>A/*MT-ATP6* (A20T)14258G>A/*MT-ND6* (P139L) | 3308T>C/*MT-ND1* (M1T)3338T>C/*MT-ND1* (V11A)6663A>G/*MT-CO1* (I254V)8584G>A/*MT-ATP6* (A20T) | 1 | Normal |
| KF451170/ HGDP00647 | XX\_XX\_6141 | U1b1 | 9374A>G/*MT-CO3* | 444A>G/*MT-DLOOP*2352T>C/*MT-RNR2* | 14258G>A/*MT-ND6* (P139L) | 15110G>A/*MT-CYB* (A122T) | 1 | Normal |
| JN203207 | EU\_PL\_0054 | U3a1a1c |  |  | 3808A>G/*MT-ND1* (T168A) | 10506A>G/*MT-ND4L* (T13A13934C>T/*MT-ND5* (T533M)14258G>A/*MT-ND6* (P139L) | 1 | Normal |
| JQ704950 | EU\_IE\_0218 | U3a1a1c | 9656T>C/*MT-CO3*14049C>T/*MT-ND5* |  |  | 10506A>G/*MT-ND4L* (T13A)13934C>T/*MT-ND5* (T533M)14258G>A/*MT-ND6* (P139L) | Normal |
| JX153017 | EU\_IT\_0472 | U3a1a1c | 13785C>T/*MT-ND5* |  |  | 10506A>G/*MT-ND4L* (T13A)13934C>T/*MT-ND5* (T533M)14258G>A/*MT-ND6* (P139L) | Normal |
| HM156692 | PA\_XX\_XX\_0032 | W3a1bd | 8251G>A*/MT-CO2* | 146T>C/*MT-HV2* | 3350T>C/*MT-ND1* (I15T)14258G>A/*MT-ND6* (P139L) | 3505A>G/*MT-ND1* (T67A)5046G>A/*MT-ND2* (V193I)15884G>C/*MT-CYB* (A380P) | 1 | Chronic Periodontitis |
| HM156696 | PA\_XX\_XX\_0028 | W3a1bd | 8251G>A/*MT-CO2*8952T>C/*MT-CO2*8994G>A/*MT-CO2* | 1243T>C/*MT-RNR1* | 3505A>G/*MT-ND1* (T67A)5460G>A/*MT-ND2* (A331T)14258G>A/*MT-ND6* (P139L) | 3505A>G/*MT-ND1* (T67A)5046G>A/*MT-ND2* (V193I)15884G>C/*MT-CYB* (A380P) | Chronic Periodontitis |

a The mutation 14258G>A/*MT-ND6* is diagnostic of haplogroup H1q3 (<http://www.phylotree.org/tree/R0.htm>). It occurred as a single mutational event in the ancestral H1q3 mitogenome.

b The two HV2a2 mitogenomes most likely harbor the mutation 14258G>A/*MT-ND6* by descent (one mutational event).

c The mutation 14258G>A/*MT-ND6* is diagnostic of haplogroup U3a1a1 (<http://www.phylotree.org/tree/U.htm>). It occurred as a single mutational event in the ancestral U3a1a1 mitogenome.

d The two W3a1b mitogenomes most likely harbor the mutation 14258G>A/*MT-ND6* by descent (one mutational event).

e The two H5b mitogenomes most likely share the mutational motif m.9966G>A/MT-CO3 (V254I), 12033A>G/MT-ND4 (N425S), 14258G>A/MT-ND6 (P139L) by descent. For the mutation 14258G>A/MT-ND6, the single mutational occurrence is further supported by its absence in all other published H5b mitogenomes.