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## Supplementary Data

# Mitochondrial DNA: hotspot for potential gene modifiers regulating hypertrophic cardiomyopathy 

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Supplementary Table S1- mtDNA variants identified by NGS in Family A composed by healthy and HCM individuals bearing the p.E99K-ACTC1 mutation.
Patients displaying more severe phenotypes/ clinical features are labelled in red; healthy or less severe patients are highlighted in green

| Fibroblast sample | Loci | mtDNA Mutation | \% Heteroplasmy | Polyphen prediction (score) |
| :---: | :---: | :---: | :---: | :---: |
| E99K1 | $\begin{gathered} \text { MT-HV2, MT- } \\ \text { OHR } \\ \hline \end{gathered}$ | m.152T>C | 99.8\% | $\begin{gathered} \mathrm{N} / \mathrm{A} \\ \text { (non-coding) } \end{gathered}$ |
| 6;7 | $\begin{gathered} \text { MT-HV2, MT- } \\ \text { OHR } \\ \hline \end{gathered}$ | m.185G>A | 98.1\%; 98.8\% | $\begin{gathered} \mathrm{N} / \mathrm{A} \\ \text { (non-coding) } \end{gathered}$ |
| E99K1; 6; 7 | $\begin{gathered} \text { MT-HV2, MT- } \\ \text { OHR, MT- } \\ \text { CSB2 } \end{gathered}$ | m.309_310insCT | 31.7\%; 32.3\%; 35.8\% | $\mathrm{N} / \mathrm{A}$ (non-coding) |
| $\begin{gathered} \text { E99K1; E99K2; NC; } \\ 6 ; 7 \end{gathered}$ | $\begin{gathered} \text { MT-HV2, MT- } \\ \text { OHR, MT- } \\ \text { CSB2 } \end{gathered}$ | m.310T>C | $\begin{gathered} 53.9 \% ; 13.5 \% ; \\ 17.2 \% ; 57.0 \% ; 58.8 \% \end{gathered}$ | $\begin{gathered} \text { N/A } \\ \text { (non-coding) } \end{gathered}$ |
| $\begin{gathered} \text { E99K1; E99K2; NC; } \\ 6 ; 7 \end{gathered}$ | $\begin{gathered} \text { MT-HV2, MT- } \\ \text { OHR, MT- } \\ \text { CSB2 } \end{gathered}$ | m.310_311insC | $\begin{gathered} 33.3 \% ; 65.8 \% ; \\ 62.5 \% ; 32.5 \% ; 31.7 \% \end{gathered}$ | $\begin{gathered} \text { N/A } \\ \text { (non-coding) } \end{gathered}$ |
| 6 | $\begin{gathered} \text { MT-OHR, MT- } \\ \text { LSP } \\ \hline \end{gathered}$ | m.414T>G | 18.7\% | $\begin{gathered} \text { N/A } \\ \text { (non-coding) } \end{gathered}$ |
| 6;7 | MT-ND2 | m. $4659 \mathrm{G}>\mathrm{A}$ | 99.7\%; 99.3\% | Benign (0.029) |
| $\begin{gathered} \text { E99K1; E99K2; NC; } \\ 6 ; 7 \end{gathered}$ | MT-TA | m.5597A>C | $\begin{gathered} 7.5 \% ; 7.9 \% ; 5.1 \% ; \\ 12.2 \% ; 12.4 \% \\ \hline \end{gathered}$ | $\begin{gathered} \text { N/A } \\ \text { (non-coding) } \end{gathered}$ |
| E99K1 | MT-CO1 | m.7109C>T | 91.4\% | N/A (redundant) |
| E99K2; NC | MT-ATP6 | m.8952T>C | 99.9\%; 99.8\% | $\mathrm{N} / \mathrm{A}$ (redundant) |
| 6;7 | MT-ATP6 | m.9025G>A | 99.6\%; 99.6\% | Probably damaging (1.000) |
| E99K1 | MT-ATP6 | $\mathrm{m} .9116 \mathrm{~T}>\mathrm{C}$ | 99.7\% | $\begin{aligned} & \text { Benign } \\ & (0.000) \\ & \hline \end{aligned}$ |
| E99K1 | MT-ND4 | m.11176G>A | 99.6\% | N/A (redundant) |
| 6;7 | MT-ND4 | m.11215C>T | 99.7\%; 99.6\% | $\mathrm{N} / \mathrm{A}$ (redundant) |
| E99K2; NC | MT-ND5 | m.12715A>G | 99.8\%; 99.8\% | Probably damaging (0.991) |
| 6;7 | MT-ND5 | m.12810A>G | 99.9\%; 99.9\% | Probably damaging (STOP) |
| 6;7 | MT-CYB | m.15586T>C | 99.8\%; 99.9\% | $\mathrm{N} / \mathrm{A}$ (redundant) |
| E99K1 | MT-HV1, MT- <br> TAS | m.16168C>T | 44.2\% | N/A (non-coding) |
| 6; 7 | MT-HV1 | m.16209T>C | 99.9\%; 99.9\% | $\begin{gathered} \mathrm{N} / \mathrm{A} \\ \text { (non-coding) } \end{gathered}$ |

Supplementary Table S2-mtDNA variants identified by NGS in Family B composed by healthy and HCM individuals bearing the p.E99K-ACTC1 mutation.
Patients displaying more severe phenotypes/ clinical features are labelled in red; healthy or less severe patients are highlighted in green.

| Fibroblast sample | Loci | mtDNA Mutation | \% heteroplasmy | Polyphen score |
| :---: | :---: | :---: | :---: | :---: |
| 4;5 | $\begin{aligned} & \text { MT-HV2, } \\ & \text { MT-OHR } \end{aligned}$ | m.152T>C | 99.8\%; 99.8\% | $\mathrm{N} / \mathrm{A}$ (non-coding) |
| $\begin{gathered} 4 ; 5 ; 13 ; 14 ; 15 ; \\ 16 ; 17 ; 18 \end{gathered}$ | MT-HV2, <br> MT-OHR, <br> MT-CSB2 | m.310T>C | $\begin{gathered} \hline 10.5 \% ; 14.3 \% ; 13.2 \% ; \\ 15.0 \% ; 13.5 \% ; 18.4 \% ; \\ 15.2 \% ; 12.9 \% \\ \hline \end{gathered}$ | $\begin{gathered} \text { N/A } \\ \text { (non-coding) } \end{gathered}$ |
| $\begin{gathered} 4 ; 5 ; 13 ; 14 ; 15 ; \\ 16 ; 17 ; 18 \end{gathered}$ | MT-HV2, <br> MT-OHR, <br> MT-CSB2 | m.310_311insC | $\begin{gathered} \hline 67.6 \% ; 67.2 \% ; 67.3 \% ; \\ 65.7 \% ; 68.6 \% ; 57.7 \% \text {; } \\ \text { 65.0\%; } 67.8 \% \\ \hline \end{gathered}$ | $\begin{gathered} \text { N/A } \\ \text { (non-coding) } \end{gathered}$ |
| 13 | MT-HV3 | m.513G>A | 13.0\% | $\mathrm{N} / \mathrm{A}$ (non-coding) |
| 14; 15; 16; 17; 18 | MT-HV3 | m.514_515delCA | $\begin{gathered} 56.3 \% ; 59.4 \% ; 55.6 \% ; \\ 55.0 \% ; 55.4 \% \\ \hline \end{gathered}$ | $\begin{gathered} \mathrm{N} / \mathrm{A} \\ \text { (non-coding) } \end{gathered}$ |
| 13 | MT-HV3 | m.513_514insCACA | 32.5\% | $\begin{gathered} \mathrm{N} / \mathrm{A} \\ \text { (non-coding) } \end{gathered}$ |
| 18 | MT-HV3, <br> MT-TFH | m.540A>C | 11.0\% | N/A (non-coding) |
| 14; 15; 16; 17; 18 | MT-HV3, MT-HSP1 | m. $567 \mathrm{~A}>\mathrm{G}$ | $\begin{gathered} \hline 99.3 \% ; 99.2 \% ; 99.2 \% ; \\ 99.5 \% ; 99.5 \% \\ \hline \end{gathered}$ | $\begin{gathered} \mathrm{N} / \mathrm{A} \\ \text { (non-coding) } \end{gathered}$ |
| 15 | MT-HV3 | m. $574 \mathrm{~A}>\mathrm{G}$ | 12.3\% | $\begin{gathered} \text { N/A } \\ \text { (non-coding) } \end{gathered}$ |
| $\begin{gathered} 4 ; 5 ; 13 ; 14 ; 15 ; \\ 16 \end{gathered}$ | MT-TA | m. $5597 \mathrm{~A}>\mathrm{C}$ | $\begin{aligned} & \hline 25.7 \% ; 10.5 \% ; 14.0 \% \text {; } \\ & 23.8 \% ; 13.8 \% ; 16.8 \% \\ & \hline \end{aligned}$ | $\begin{gathered} \mathrm{N} / \mathrm{A} \\ \text { (non-coding) } \end{gathered}$ |
| 4 | MT-ATP8 | m. $8490 \mathrm{~T}>\mathrm{A}$ | 10.0\% | Possibly damaging (0.711) |
| 4; 5; 14 | MT-CO3 | m.9716T>C | 100\%; 99.9\%; 2.4\% | N/A (redundant) |
| 4; 5; 14 | MT-ND4 | m.11914G>A | 99.8\%; 99.4\%; 1.9\% | N/A (redundant) |
| 14; 15; 16; 17; 18 | MT-ND4 | m.11950A>G | $\begin{gathered} \hline 97.9 \% ; 99.8 \% ; 99.8 \% ; \\ 99.8 \% ; 99.9 \% \\ \hline \end{gathered}$ | $\mathrm{N} / \mathrm{A}$ (redundant) |
| 4 | MT-CYB | m.15639T>C | 18.4\% | Probably damaging (0.998) |
| 4; 5; 14 | MT-CYB | m.15670T>C | 99.8\%; 99.9\%; 2.1\% | $\begin{gathered} \hline \mathrm{N} / \mathrm{A} \\ \text { (redundant) } \end{gathered}$ |
| 4 | MT-HV1 | m.16390G>A | 12.7\% | $\begin{gathered} \text { N/A } \\ \text { (non-coding) } \end{gathered}$ |

Supplementary Table S3-mtDNA variants identified by NGS in Family C composed by healthy and HCM individuals bearing the p.E99K-ACTC1 mutation.
Patients displaying more severe phenotypes/ clinical features are labelled in red; healthy or less severe patients are highlighted in green.

| Fibroblast <br> sample | Loci | mtDNA Position | \% heteroplasmy | Polyphen <br> prediction <br> (score) |
| :---: | :---: | :---: | :---: | :---: |
| $8 ; 9 ; 10$ | MT-HV2, MT- <br> OHR, MT-CSB2 | m.310T>C | $16.0 \% ; 11.0 \% ;$ <br> $14.0 \%$ | N/A <br> (non-coding) |
| $8 ; 9 ; 10$ | MT-HV2, MT- <br> OHR, MT-CSB2 | m.310_311insC | $67.1 \% ; 69.6 \% ;$ <br> $70.1 \%$ | N/A <br> (non-coding) |
| $8 ; 9 ; 10$ | MT-HV3 | m.513G>A | $11.9 \% ; 14.8 \% ; 9.9 \%$ | N/A <br> (non-coding) |
| $8 ; 9 ; 10$ | MT-HV3 | m.513_514insCACA | $31.9 \% ; 33.3 \% ;$ <br> $34.9 \%$ | N/A <br> (non-coding) |
| $8 ; 10$ | MT-TA | m.5597A>C | $11.2 \% ; 10.7 \%$ | N/A <br> (non-coding) |

Supplementary Table S4-Analysis of m.152T>C mtDNA variant frequency in haplogroups (number between brackets) using full length sequence set (left) or control region sequence set (right) deposited in MITOMAP database.

| Using Full Length sequence set |  |  |  |
| :---: | :---: | :---: | :---: |
|  |  |  |  |
| Top <br> Level <br> HG | Top Level <br> HG Branch <br> (ltr-num) | HG Branch (ltr- <br> num-ltr) |  |
|  |  |  |  |


| Using Control Region sequence set |  |  |  |
| :---: | :---: | :---: | :---: |
| Lineage | Top Level HG | Top Level HG Branch (ltr-num) | HG Branch (ltr-num-ltr) |
| $\begin{aligned} & \text { L } 4405 \\ & (52.5 \%) \end{aligned}$ | L0 | L0 | L0f 50 (71.4\%) |
|  |  |  | L0k 70 (69.3\%) |
|  | $\begin{aligned} & \text { L1 1057 } \\ & \text { (88.3\%) } \end{aligned}$ | $\begin{aligned} & \text { L1 1057 } \\ & (88.3 \%) \end{aligned}$ | $\begin{aligned} & \text { L1b } 523 \\ & (87.5 \%) \end{aligned}$ |
|  |  |  | L1c 534 (89.4\%) |
|  | $\begin{aligned} & \text { L2 } 1763 \\ & (82.0 \%) \end{aligned}$ | $\begin{aligned} & \text { L2 } 1755 \\ & (81.6 \%) \end{aligned}$ | $\begin{gathered} \text { L2a } 1265 \\ (83.8 \%) \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { L2b } 225 \\ & (89.3 \%) \end{aligned}$ |
|  |  |  | L2c 234 (84.2\%) |
|  |  |  | L2e 28 (68.3\%) |
|  | L3 | L3 | L3a 21 (56.8\%) |
|  |  |  | $\begin{aligned} & \text { L3d } 388 \\ & (72.7 \%) \end{aligned}$ |
|  |  |  | L3k 16 (66.7\%) |
| $\begin{aligned} & \text { M } 2598 \\ & (11.1 \%) \end{aligned}$ | C | C4 | C4 54 (100.0\%) |
|  |  |  | C4e 12 (66.7\%) |
|  | D | D4 | $\begin{aligned} & \text { D4a } 306 \\ & (57.3 \%) \end{aligned}$ |
|  |  | D5 | D5 16 (76.2\%) |
|  |  |  | D5c 24 (85.7\%) |
|  |  | D6 | $\begin{gathered} \hline \text { D6c } 44 \\ (100.0 \%) \\ \hline \end{gathered}$ |
|  | M | M3 | M3c 43 (67.2\%) |
|  |  | M4 | M4b 9 (50.0\%) |


|  | D5 | D5c 18 (100.0\%) |
| :---: | :---: | :---: |
|  | D6 | D6c 12 (100.0\%) |
|  | M2 | M2b 98 (96.1\%) |


|  |  | M13 | $\begin{gathered} \text { M13 } 59 \\ (100.0 \%) \\ \hline \end{gathered}$ |
| :---: | :---: | :---: | :---: |
|  |  | M13 | $\begin{gathered} \hline \text { M13c } 19 \\ (76.0 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{aligned} & \text { M23 23 } \\ & \text { (74.2\%) } \end{aligned}$ | M23 23 (74.2\%) |
|  |  | M24 | $\begin{gathered} \text { M24a } 13 \\ (86.7 \%) \\ \hline \end{gathered}$ |
|  |  | M30 | $\begin{aligned} & \text { M30b } 14 \\ & (100.0 \%) \\ & \hline \end{aligned}$ |
|  |  | $\begin{aligned} & \text { M36 } 19 \\ & (63.3 \%) \end{aligned}$ | $\begin{aligned} & \hline \text { M36a } 13 \\ & (100.0 \%) \end{aligned}$ |
|  |  | $\begin{aligned} & \text { M37 18 } \\ & \text { (56.2\%) } \end{aligned}$ | M37 17 (89.5\%) |
|  |  | $\begin{aligned} & \text { M57 } 14 \\ & (93.3 \%) \end{aligned}$ |  |
|  |  | M74 | M74 7 (50.0\%) |
|  |  | $\begin{aligned} & \text { M75 } 16 \\ & (61.5 \%) \end{aligned}$ | M75 16 (61.5\%) |
|  |  |  | Z3 17 (100.0\%) |
|  | $\text { Z } 311$ |  | Z3a 34 (89.5\%) |
|  |  |  | Z4 27 (100.0\%) |
|  |  |  | Z4a 47 (54.0\%) |
|  |  | A2 | A2v 12 (80.0\%) |
|  |  | A5 | A5c 10 (58.8\%) |
|  |  | A6 23 (92.0\%) | A6b 16 (88.9\%) |
|  |  | A7 14 (63.6\%) | A7 14 (63.6\%) |
| N 5863 | A | A11 | $\begin{aligned} & \text { A11b } 14 \\ & (100.0 \%) \\ & \hline \end{aligned}$ |
| (14.1\%) | A | $\begin{aligned} & \text { A14 112 } \\ & (100.0 \%) \end{aligned}$ | $\begin{aligned} & \text { A14 } 112 \\ & (100.0 \%) \\ & \hline \end{aligned}$ |
|  |  | A15 152 | $\begin{gathered} \hline \text { A15 141 } \\ (98.6 \%) \\ \hline \end{gathered}$ |
|  |  | (93.3\%) | $\begin{gathered} \hline \text { A15b } 11 \\ (55.0 \%) \\ \hline \end{gathered}$ |
|  |  | A16 8 (61.5\%) | A16 8 (61.5\%) |
|  |  | $\begin{gathered} \text { A24 10 } \\ (100.0 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \text { A24 10 } \\ (100.0 \%) \\ \hline \end{gathered}$ |


|  |  |  | Z3b 8 (80.0\%) |
| :---: | :---: | :---: | :---: |
|  |  | $\begin{gathered} \hline \text { Z4 26 } \\ (100.0 \%) \\ \hline \end{gathered}$ | Z4a 17 (100.0\%) |
| $\begin{aligned} & \text { N } 7119 \\ & (21.4 \%) \end{aligned}$ | A | A | A 57 (86.4\%) |
|  |  | $\begin{gathered} \text { A1 } 13 \\ (100.0 \%) \\ \hline \end{gathered}$ | A1a 12 (100.0\%) |
|  |  | A2 | A2v 10 (90.9\%) |
|  |  | $\begin{gathered} \text { A6 16 } \\ (100.0 \%) \end{gathered}$ |  |
|  |  | A8 | A8a 10 (62.5\%) |
|  |  | $\begin{aligned} & \text { A11 34 } \\ & (97.1 \%) \end{aligned}$ | A11a 22 (95.7\%) |
|  |  |  | $\begin{aligned} & \hline \text { A11b } 10 \\ & (100.0 \%) \\ & \hline \end{aligned}$ |
|  |  | $\begin{gathered} \text { A12 12 } \\ (100.0 \%) \end{gathered}$ | $\begin{aligned} & \hline \text { A12a } 10 \\ & (100.0 \%) \end{aligned}$ |
|  |  | $\begin{gathered} \hline \text { A13 19 } \\ (100.0 \%) \\ \hline \end{gathered}$ | A13 19 (100.0\%) |
|  |  | $\begin{array}{r} \text { A14 34 } \\ (94.4 \%) \\ \hline \end{array}$ | A14 34 (94.4\%) |
|  |  | $\begin{aligned} & \text { A15 } 67 \\ & \text { (97.1\%) } \end{aligned}$ | $\begin{aligned} & \hline \text { A15a 10 } \\ & (100.0 \%) \\ & \hline \end{aligned}$ |
|  |  |  | A15c 53 (98.1\%) |
|  |  | $\begin{aligned} & \hline \text { A17 } 40 \\ & (95.2 \%) \\ & \hline \end{aligned}$ | A17 40 (95.2\%) |
|  | B | B2 | B2q 15 (71.4\%) |
|  | F | F1 | F1b 93 (66.9\%) |
|  |  |  | F1c 46 (97.9\%) |
|  |  | $\begin{aligned} & \hline \text { F3 162 } \\ & (54.9 \%) \\ & \hline \end{aligned}$ | F3b 155 (68.6\%) |
|  |  | F4 | F4a 18 (56.2\%) |
|  | H | H1 | H1i 17 (89.5\%) |
|  |  | H2 | H2b 28 (96.6\%) |
|  |  | H3 | H3g 58 (96.7\%) |
|  |  |  | H3k 17 (100.0\%) |
|  |  |  | H3q 6 (54.5\%) |
|  |  | H8 | H8c 22 (95.7\%) |


|  | A25 7 (70.0\%) | A25 7 (70.0\%) |
| :---: | :---: | :---: |
| B | B2 | B2b 83 (85.6\%) |
|  |  | B2u 6 (60.0\%) |
| F | F2 | F2i 14 (58.3\%) |
| H | $\begin{gathered} \text { H9 22 } \\ (100.0 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \hline \text { H9a } 22 \\ (100.0 \%) \\ \hline \end{gathered}$ |
|  | $\begin{gathered} \hline \text { H32 62 } \\ (100.0 \%) \end{gathered}$ | $\begin{gathered} \hline \text { H32 62 } \\ (100.0 \%) \end{gathered}$ |
|  | $\begin{aligned} & \text { H36 } 12 \\ & (70.6 \%) \end{aligned}$ | H36 12 (70.6\%) |
| HV | HV1 | $\begin{gathered} \text { HV1b } 23 \\ (50.0 \%) \end{gathered}$ |
|  | $\begin{aligned} & \hline \text { HV2 } 58 \\ & (65.9 \%) \\ & \hline \end{aligned}$ | $\begin{gathered} \text { HV2a } 38 \\ (84.4 \%) \end{gathered}$ |
| I | I2 27 (71.1\%) | I2 24 (80.0\%) |
|  | I3 11 (68.8\%) | I3a 11 (68.8\%) |
| J | J1 | J1d 84 (52.2\%) |
|  | J2 219 (58.1\%) | J2b 126 (84.0\%) |
| K | K1 | $\begin{aligned} & \text { K1c } 145 \\ & (91.2 \%) \\ & \hline \end{aligned}$ |
|  | K2 | K2a 50 (69.4\%) |
| N | N1 | $\begin{aligned} & \hline \text { N1b } 123 \\ & (52.1 \%) \\ & \hline \end{aligned}$ |
| R | R2 63 (61.8\%) | R2 52 (61.9\%) |
|  |  | R2b 10 (76.9\%) |
|  | R7 15 (51.7\%) | R7 9 (81.8\%) |
| S | S | S 22 (100.0\%) |
| T | T2 | T2d 20 (69.0\%) |
| U | U2 | U2c 45 (68.2\%) |
|  |  | $\begin{aligned} & \text { U2e } 170 \\ & (63.7 \%) \end{aligned}$ |
|  | $\begin{aligned} & \text { U7 } 269 \\ & (59.1 \%) \\ & \hline \end{aligned}$ | $\begin{aligned} & \text { U7a } 208 \\ & (79.1 \%) \\ & \hline \end{aligned}$ |
|  | U8 | U8c 8 (61.5\%) |
| X | X4 8 (72.7\%) | X4 8 (72.7\%) |




Supplementary Table S5-Analysis of m.309_310insCT mtDNA variant frequency in haplogroups (number between brackets) using full length sequence set (left) or control region sequence set (right) deposited in MITOMAP database.

| Using Full Length sequence set |  |  |  |
| :---: | :---: | :---: | :---: |
| Lineage | Top <br> Level <br> HG | Top Level HG Branch (ltr-num) | HG Branch <br> (ltr-num-ltr) |
| $\begin{gathered} \hline \text { L } 1001 \\ (16.2 \%) \end{gathered}$ | $\begin{gathered} \hline \text { L6 } 7 \\ (58.3 \%) \\ \hline \end{gathered}$ | L6 7 (58.3\%) |  |
| $\begin{aligned} & \text { M } 3220 \\ & (30.1 \%) \end{aligned}$ | C | C | C 243 (54.0\%) |
|  |  | $\begin{aligned} & \text { C1 161 } \\ & (51.6 \%) \end{aligned}$ | $\begin{aligned} & \text { C1b 65 } \\ & \text { (51.6\%) } \end{aligned}$ |
|  |  |  | C1c 32 (54.2\%) |
|  |  |  | $\begin{aligned} & \text { C1d } 61 \\ & (50.8 \%) \end{aligned}$ |
|  | D | D1 | D1j 12 (57.1\%) |
|  |  | D2 50 (58.1\%) | $\begin{aligned} & \text { D2a } 41 \\ & (65.1 \%) \end{aligned}$ |
|  |  |  | D2b 9 (60.0\%) |
|  |  | D4 | D4s 9 (69.2\%) |
|  | M | M1 | $\begin{aligned} & \text { M1b } 15 \\ & \text { (50.0\%) } \end{aligned}$ |
|  |  | M5 | $\begin{aligned} & \text { M5b } 16 \\ & (57.1 \%) \end{aligned}$ |
|  |  | $\begin{aligned} & \text { M11 19 } \\ & \text { (50.0\%) } \end{aligned}$ | $\begin{aligned} & \text { M11b } 7 \\ & (70.0 \%) \end{aligned}$ |
|  |  | M13 | $\begin{aligned} & \text { M13c } 8 \\ & (61.5 \%) \end{aligned}$ |
|  |  | M21 | $\begin{gathered} \hline \text { M21a } 18 \\ (54.5 \%) \\ \hline \end{gathered}$ |
|  |  | M33 | $\begin{array}{r} \text { M33a } 27 \\ (67.5 \%) \\ \hline \end{array}$ |
|  |  | M34 6 (60.0\%) |  |
|  |  | M35 | M35b 41 <br> (71.9\%) |
|  |  | $\begin{aligned} & \text { M36 30 } \\ & \text { (78.9\%) } \end{aligned}$ | $\begin{gathered} \hline \text { M36d } 23 \\ (82.1 \%) \\ \hline \end{gathered}$ |


| Using Control Region sequence set |  |  |  |
| :---: | :---: | :---: | :---: |
| Lineage | Top Level HG | Top Level HG Branch (ltr-num) | HG Branch (ltr-num-ltr) |
| $\begin{gathered} \hline \text { L } 1640 \\ (19.5 \%) \end{gathered}$ | L4 | L4 | L4 6 (50.0\%) |
| $\begin{aligned} & \text { M } 4047 \\ & (17.3 \%) \end{aligned}$ | C | C4 | C4e 9 (50.0\%) |
|  | D | $\begin{aligned} & \text { D2 129 } \\ & (64.2 \%) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline \text { D2c } 127 \\ & (72.2 \%) \\ & \hline \end{aligned}$ |
|  |  | D4 | D4 22 (59.5\%) |
|  |  | D5 | $\begin{gathered} \text { D5c } 16 \\ (57.1 \%) \end{gathered}$ |
|  |  | D6 | $\begin{aligned} & \hline \text { D6c } 25 \\ & (56.8 \%) \\ & \hline \end{aligned}$ |
|  | M | M5 | $\begin{aligned} & \text { M5c } 14 \\ & (51.9 \%) \\ & \hline \end{aligned}$ |
|  |  | M10 | M10 8 (72.7\%) |
|  |  | M11 | $\begin{aligned} & \text { M11 17 } \\ & \text { (70.8\%) } \end{aligned}$ |
|  |  | M13 | $\begin{aligned} & \text { M13 } 46 \\ & (78.0 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{gathered} \text { M13c } 20 \\ (80.0 \%) \end{gathered}$ |
|  |  | $\begin{gathered} \text { M38 } 6 \\ (50.0 \%) \\ \hline \end{gathered}$ |  |
|  |  | M65 | $\begin{aligned} & \text { M65b } 7 \\ & (58.3 \%) \end{aligned}$ |
|  |  | M74 | M74 8 (57.1\%) |
|  |  | M91 | $\begin{aligned} & \text { M91a } 7 \\ & (50.0 \%) \end{aligned}$ |
|  | Q | Q1 | $\begin{aligned} & \text { Q1a } 37 \\ & (50.0 \%) \end{aligned}$ |
|  | Z | $\begin{gathered} \text { Z3 } 34 \\ (54.8 \%) \\ \hline \end{gathered}$ | $\begin{array}{r} \text { Z3a } 23 \\ (60.5 \%) \\ \hline \end{array}$ |
|  |  | Z4 | Z4 17 (63.0\%) |


|  |  | $\begin{aligned} & \text { M38 } 13 \\ & (56.5 \%) \\ & \hline \end{aligned}$ |  |
| :---: | :---: | :---: | :---: |
|  |  | M52 | $\begin{aligned} & \hline \text { M52b } 8 \\ & (57.1 \%) \end{aligned}$ |
|  |  | $\begin{aligned} & \hline \text { M57 10 } \\ & \text { (71.4\%) } \\ & \hline \end{aligned}$ |  |
|  |  | M62 | $\begin{gathered} \text { M62b } 10 \\ (55.6 \%) \end{gathered}$ |
|  |  | M73 | M73 6 (54.5\%) |
| $\begin{aligned} & \text { N } 9019 \\ & (27.1 \%) \end{aligned}$ | A | A2 | $\begin{gathered} \hline \text { A2a } 118 \\ (52.2 \%) \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { A2b } 22 \\ & (51.2 \%) \\ & \hline \end{aligned}$ |
|  |  |  | A2p 7 (50.0\%) |
|  |  |  | $\begin{aligned} & \text { A2w } 11 \\ & (50.0 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { A2y } 12 \\ & (80.0 \%) \end{aligned}$ |
|  |  | A5 63 (60.0\%) | $\begin{aligned} & \text { A5a } 53 \\ & (80.3 \%) \\ & \hline \end{aligned}$ |
|  |  | $\begin{aligned} & \hline \text { A13 11 } \\ & (57.9 \%) \end{aligned}$ | $\begin{aligned} & \text { A13 11 } \\ & \text { (57.9\%) } \end{aligned}$ |
|  | B | B2 | B2d 7 (58.3\%) |
|  |  |  | B21 7 (50.0\%) |
|  | H | H1 | $\begin{aligned} & \text { H1h } 11 \\ & (55.0 \%) \end{aligned}$ |
|  |  |  | H1r 6 (60.0\%) |
|  |  |  | H1v 8 (50.0\%) |
|  |  | H7 | $\begin{aligned} & \mathrm{H} 7 \mathrm{a} 29 \\ & (52.7 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { H7e } 16 \\ & (66.7 \%) \\ & \hline \end{aligned}$ |
|  |  | H10 | $\begin{gathered} \hline \text { H10e } 39 \\ (61.9 \%) \\ \hline \end{gathered}$ |
|  |  | H31 | $\begin{gathered} \text { H31a } 10 \\ (76.9 \%) \end{gathered}$ |
|  |  | $\begin{array}{r} \text { H35 } 14 \\ (60.9 \%) \\ \hline \end{array}$ | $\begin{aligned} & \text { H35 } 11 \\ & (55.0 \%) \\ & \hline \end{aligned}$ |
|  |  | H40 7 (53.8\%) |  |
|  |  | H49 | $\begin{gathered} \text { H49a } 12 \\ (57.1 \%) \end{gathered}$ |
|  |  | H51 6 (54.5\%) |  |
|  |  | H52 8 (61.5\%) | H52 8 (61.5\%) |


| $\begin{aligned} & \text { N } 6358 \\ & (15.3 \%) \end{aligned}$ | A | A2 | $\begin{aligned} & \text { A2g } 10 \\ & (71.4 \%) \end{aligned}$ |
| :---: | :---: | :---: | :---: |
|  |  |  | $\begin{aligned} & \mathrm{A} 2 \mathrm{~m} 12 \\ & (66.7 \%) \end{aligned}$ |
|  |  | A11 | $\begin{aligned} & \text { A11b } 8 \\ & (57.1 \%) \end{aligned}$ |
|  |  | $\begin{gathered} \text { A24 } 7 \\ (70.0 \%) \end{gathered}$ | A24 7 (70.0\%) |
|  | HV | $\begin{gathered} \text { HV14 } 22 \\ (62.9 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \hline \text { HV14 } 22 \\ (62.9 \%) \\ \hline \end{gathered}$ |
|  | S | S | S 11 (50.0\%) |
|  | W | $\begin{gathered} \text { W3 } 34 \\ (61.8 \%) \end{gathered}$ | $\begin{aligned} & \text { W3a } 32 \\ & (60.4 \%) \end{aligned}$ |


| HV | HV0 | $\begin{aligned} & \text { HV0d } 7 \\ & (53.8 \%) \end{aligned}$ |
| :---: | :---: | :---: |
|  | $\begin{aligned} & \hline \text { HV4 } 56 \\ & (58.3 \%) \end{aligned}$ | $\begin{gathered} \hline \text { HV4a } 47 \\ (67.1 \%) \\ \hline \end{gathered}$ |
|  | HV9 | HV9 8 (53.3\%) |
|  | $\begin{gathered} \text { HV14 } 46 \\ (80.7 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \text { HV14a } 45 \\ (81.8 \%) \\ \hline \end{gathered}$ |
|  | $\begin{gathered} \hline \text { HV16 } 10 \\ (66.7 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \hline \text { HV16 10 } \\ (66.7 \%) \\ \hline \end{gathered}$ |
| I | I1 | I1 11 (52.4\%) |
|  |  | I1b 19 (51.4\%) |
|  |  | I1c 7 (50.0\%) |
|  | I2 | I2a 13 (50.0\%) |
|  | I3 38 (58.5\%) | I3a 23 (63.9\%) |
|  |  | I3d 6 (50.0\%) |
| N | N2 7 (63.6\%) | N2a 7 (63.6\%) |
|  | N7 8 (57.1\%) |  |
| P | P9 7 (63.6\%) |  |
| R | R2 | $\begin{aligned} & \text { R2d } 10 \\ & (58.8 \%) \\ & \hline \end{aligned}$ |
|  | R8 64 (63.4\%) | $\begin{aligned} & \text { R8b } 42 \\ & (87.5 \%) \\ & \hline \end{aligned}$ |
| T | T1 | T1b 25 (62.5\%) |
|  | T2 | T2n 7 (70.0\%) |
| U | U7 | $\begin{aligned} & \text { U7b } 61 \\ & (53.5 \%) \\ & \hline \end{aligned}$ |
|  | U8 | $\begin{aligned} & \text { U8a } 57 \\ & (61.3 \%) \end{aligned}$ |
|  | U9 9 (56.2\%) |  |
| V | V5 7 (70.0\%) | V5 7 (70.0\%) |
|  | $\begin{array}{r} \text { V10 } 15 \\ (62.5 \%) \\ \hline \end{array}$ | V10a 9 (81.8\%) |
|  | V12 6 (60.0\%) | V12 6 (60.0\%) |
|  | V22 6 (50.0\%) | V22 6 (50.0\%) |
| W | W1 | $\begin{aligned} & \text { W1b } 15 \\ & (57.7 \%) \end{aligned}$ |
|  | $\begin{aligned} & \text { W3 } 72 \\ & (52.2 \%) \end{aligned}$ | W3a 46 (50.0\%) |
|  |  | $\begin{aligned} & \text { W3b } 25 \\ & (58.1 \%) \\ & \hline \end{aligned}$ |
|  | $\begin{aligned} & \text { W6 } 46 \\ & (54.1 \%) \end{aligned}$ | $\begin{aligned} & \text { W6a } 11 \\ & (55.0 \%) \end{aligned}$ |
| X | X2 | X2p 6 (60.0\%) |

Supplementary Table S6-Analysis of m.309_310insCCT mtDNA variant frequency in haplogroups (number between brackets) using full length sequence set (left) or control region sequence set (right) deposited in MITOMAP database.

| Using Full Length sequence set |  |  |  |
| :---: | :---: | :---: | :---: |
| Lineage | Top Level HG | Top Level HG <br> Branch <br> (ltr-num) | HG Branch (ltr-numltr) |
| $\begin{aligned} & \text { M } 689 \\ & (6.4 \%) \end{aligned}$ | M | $\begin{gathered} \text { M50 } 9 \\ (50.0 \%) \\ \hline \end{gathered}$ | $\begin{aligned} & \text { M50a } 8 \\ & (61.5 \%) \end{aligned}$ |
|  |  | $\begin{aligned} & \text { M53 } 17 \\ & (65.4 \%) \end{aligned}$ | $\begin{gathered} \text { M53b } 16 \\ (69.6 \%) \end{gathered}$ |


| Using Control Region sequence set |  |  |  |
| :---: | :---: | :---: | :---: |
| Lineage | Top <br> Level <br> HG | Top Level <br> HG Branch <br> (ltr-num) | HG Branch <br> (ltr-num-ltr) |
|  | B | B2 | B2y 30 (54.5\%) |
|  | H | H66 13 <br> $(50.0 \%)$ | H66a 13 <br> $(50.0 \%)$ |

Supplementary Table S7-Analysis of m.310T>C mtDNA variant frequency in haplogroups (number between brackets) using full length sequence set (left) or control region sequence set (right) deposited in MITOMAP database.

| Using Full Length sequence set |  |  |  |
| :---: | :---: | :---: | :---: |
| Lineage | Top Level HG | Top <br> Level <br> HG <br> Branch (ltrnum) | HG Branch (ltr-numltr) |
| $\begin{gathered} \text { L } 2092 \\ (33.8 \%) \end{gathered}$ | L2 | L2 | $\begin{gathered} \text { L2e } 9 \\ (52.9 \%) \end{gathered}$ |
|  | $\begin{gathered} \text { L6 } 7 \\ (58.3 \%) \end{gathered}$ | $\begin{gathered} \text { L6 } 7 \\ (58.3 \%) \end{gathered}$ |  |
| $\begin{aligned} & \text { M } 4436 \\ & (41.4 \%) \end{aligned}$ | C | C | $\begin{gathered} \text { C } 297 \\ (66.0 \%) \end{gathered}$ |
|  |  | $\begin{aligned} & \text { C1 187 } \\ & (59.9 \%) \end{aligned}$ | $\begin{aligned} & \text { C1b } 74 \\ & (58.7 \%) \end{aligned}$ |
|  |  |  | $\begin{gathered} \text { C1c } 44 \\ (74.6 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { C1d } 66 \\ & (55.0 \%) \end{aligned}$ |
|  |  | C4 | $\begin{gathered} \text { C4 } 15 \\ (51.7 \%) \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { C4c } 23 \\ & (69.7 \%) \end{aligned}$ |
|  | D | D1 | $\begin{gathered} \text { D1j } 13 \\ (61.9 \%) \end{gathered}$ |
|  |  | $\begin{gathered} \text { D2 } 53 \\ (61.6 \%) \end{gathered}$ | $\begin{aligned} & \text { D2a } 42 \\ & (66.7 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { D2b } 10 \\ & (66.7 \%) \end{aligned}$ |
|  |  | D4 | $\begin{gathered} \text { D4 36 } \\ (51.4 \%) \end{gathered}$ |
|  |  |  | $\begin{aligned} & \hline \text { D4a } 88 \\ & (56.8 \%) \end{aligned}$ |
|  |  |  | $\begin{gathered} \hline \text { D4b } 136 \\ (55.3 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{aligned} & \mathrm{D} 4 \mathrm{~g} 44 \\ & (54.3 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \hline \text { D4o } 29 \\ & (54.7 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{gathered} \text { D4s } 9 \\ (69.2 \%) \end{gathered}$ |
|  |  | D6 | $\begin{gathered} \hline \text { D6c } 7 \\ (58.3 \%) \\ \hline \end{gathered}$ |


| Using Control Region sequence set |  |  |  |
| :---: | :---: | :---: | :---: |
| Lineage | Top Level HG | Top <br> Level HG <br> Branch <br> (ltr-num) | HG Branch <br> (ltr-num-ltr) |
| $\begin{gathered} \text { L 1878 } \\ (22.4 \%) \end{gathered}$ | L4 | L4 | L4 7 (58.3\%) |
| $\begin{aligned} & \text { M } 6220 \\ & (26.6 \%) \end{aligned}$ | C | C4 | $\begin{aligned} & \text { C4e } 10 \\ & (55.6 \%) \\ & \hline \end{aligned}$ |
|  |  | C7 | C7 21 (50.0\%) |
|  | D | D1 | D1 63 (56.2\%) |
|  |  |  | $\begin{aligned} & \hline \text { D1a 17 } \\ & (85.0 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { D1e } 19 \\ & (51.4 \%) \end{aligned}$ |
|  |  |  | $\begin{gathered} \text { D1f } 19 \\ (59.4 \%) \end{gathered}$ |
|  |  | $\begin{aligned} & \hline \text { D2 178 } \\ & \text { (88.6\%) } \end{aligned}$ | $\begin{aligned} & \hline \text { D2c } 176 \\ & (100.0 \%) \end{aligned}$ |
|  |  | D4 | D4 26 (70.3\%) |
|  |  |  | $\begin{aligned} & \hline \text { D4g } 91 \\ & (54.2 \%) \end{aligned}$ |
|  |  | D5 | D5 11 (52.4\%) |
|  |  |  | $\begin{gathered} \text { D5c } 21 \\ (75.0 \%) \\ \hline \end{gathered}$ |
|  |  | D6 | $\begin{gathered} \hline \text { D6c } 30 \\ (68.2 \%) \\ \hline \end{gathered}$ |
|  | G | G | G 24 (77.4\%) |
|  | M | M3 | $\begin{aligned} & \text { M3c } 33 \\ & (51.6 \%) \\ & \hline \end{aligned}$ |
|  |  | M5 | $\begin{aligned} & \text { M5c } 15 \\ & (55.6 \%) \\ & \hline \end{aligned}$ |
|  |  | M9 | $\begin{aligned} & \text { M9 159 } \\ & (68.2 \%) \\ & \hline \end{aligned}$ |
|  |  | M10 | M10 9 (81.8\%) |



|  |  | M42 | $\begin{gathered} \text { M42b } 10 \\ (55.6 \%) \end{gathered}$ |
| :---: | :---: | :---: | :---: |
|  |  | $\begin{gathered} \text { M44 } 8 \\ (66.7 \%) \end{gathered}$ | $\begin{aligned} & \text { M44a } 7 \\ & (63.6 \%) \end{aligned}$ |
|  |  | $\begin{aligned} & \text { M45 } 18 \\ & (64.3 \%) \end{aligned}$ | $\begin{gathered} \text { M45a } 11 \\ (57.9 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{aligned} & \text { M46 } 10 \\ & (83.3 \%) \end{aligned}$ |  |
|  |  | $\begin{aligned} & \text { M50 } 15 \\ & \text { (83.3\%) } \end{aligned}$ | $\begin{gathered} \text { M50a } 12 \\ (92.3 \%) \\ \hline \end{gathered}$ |
|  |  | M52 | $\begin{gathered} \hline \text { M52b } 11 \\ (78.6 \%) \end{gathered}$ |
|  |  | $\begin{aligned} & \text { M53 } 23 \\ & (88.5 \%) \end{aligned}$ | $\begin{gathered} \hline \text { M53b } 22 \\ (95.7 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{gathered} \text { M54 6 } \\ (54.5 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \text { M54 } 6 \\ (54.5 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{aligned} & \text { M57 11 } \\ & (78.6 \%) \end{aligned}$ |  |
|  |  | $\begin{aligned} & \text { M61 14 } \\ & (53.8 \%) \end{aligned}$ |  |
|  |  | $\begin{aligned} & \text { M62 } 18 \\ & (81.8 \%) \\ & \hline \end{aligned}$ | $\begin{gathered} \hline \text { M62b } 15 \\ (83.3 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{aligned} & \text { M71 48 } \\ & (51.6 \%) \end{aligned}$ | $\begin{gathered} \hline \text { M71a } 27 \\ (62.8 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{aligned} & \text { M72 } 10 \\ & (52.6 \%) \end{aligned}$ | $\begin{aligned} & \text { M72a } 9 \\ & (60.0 \%) \end{aligned}$ |
|  |  | $\begin{aligned} & \text { M73 } 14 \\ & (56.0 \%) \\ & \hline \end{aligned}$ | $\begin{gathered} \text { M73 } 8 \\ (72.7 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{aligned} & \text { M76 } 15 \\ & (60.0 \%) \\ & \hline \end{aligned}$ | $\begin{aligned} & \text { M76 13 } \\ & (81.2 \%) \end{aligned}$ |
|  |  | $\begin{aligned} & \text { M91 } 16 \\ & (69.6 \%) \end{aligned}$ | $\begin{gathered} \text { M91a } 12 \\ (66.7 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{gathered} \text { Z1 } 50 \\ (56.8 \%) \\ \hline \end{gathered}$ | $\begin{aligned} & \text { Z1a } 49 \\ & (57.0 \%) \end{aligned}$ |
|  | Z | Z3 | $\begin{aligned} & \text { Z3a } 17 \\ & (77.3 \%) \\ & \hline \end{aligned}$ |
|  |  | Z4 | $\begin{gathered} \text { Z4a } 9 \\ (52.9 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { A2 } 198 \\ & \text { (55.9\%) } \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { A2a 163 } \\ & (72.1 \%) \\ & \hline \end{aligned}$ |
| $\begin{gathered} \text { N } 13904 \\ (41.8 \%) \end{gathered}$ | $\begin{gathered} \text { A } 776 \\ (55.6 \%) \end{gathered}$ | $\begin{aligned} & \text { A2 } 546 \\ & (61.0 \%) \end{aligned}$ | $\begin{aligned} & \text { A2b } 26 \\ & (60.5 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { A2d } 15 \\ & (60.0 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{aligned} & \mathrm{A} 2 \mathrm{~g} 11 \\ & (84.6 \%) \end{aligned}$ |


|  |  | A11 | $\begin{aligned} & \text { A11b } 9 \\ & (64.3 \%) \\ & \hline \end{aligned}$ |
| :---: | :---: | :---: | :---: |
|  |  | A15 109 | $\begin{aligned} & \hline \text { A15 99 } \\ & (69.2 \%) \end{aligned}$ |
|  |  | (66.9\%) | A15b 10 $(50.0 \%)$ |
|  |  | $\begin{gathered} \text { A24 } 8 \\ (80.0 \%) \end{gathered}$ | A24 8 (80.0\%) |
|  | B | $\begin{gathered} \text { B2 } 384 \\ (61.8 \%) \end{gathered}$ | B2 11 (68.8\%) |
|  |  |  | $\begin{aligned} & \text { B2a 119 } \\ & (74.8 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{gathered} \text { B2b } 63 \\ (64.9 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{gathered} \text { B2c } 64 \\ (69.6 \%) \end{gathered}$ |
|  |  |  | $\begin{gathered} \text { B2y } 51 \\ (92.7 \%) \\ \hline \end{gathered}$ |
|  |  | B4 | $\begin{gathered} \text { B4e } 10 \\ (62.5 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { B4m } 42 \\ & (66.7 \%) \\ & \hline \end{aligned}$ |
|  |  | B6 | B6 8 (53.3\%) |
|  | F | F | F 17 (68.0\%) |
|  |  | F2 | F2i 12 (50.0\%) |
|  | H | H1 | $\begin{aligned} & \text { H1u } 10 \\ & \text { (71.4\%) } \end{aligned}$ |
|  |  | H5 | $\begin{aligned} & \mathrm{H} 5 \mathrm{~b} 25 \\ & (65.8 \%) \end{aligned}$ |
|  |  |  | H5n 5 (50.0\%) |
|  |  | H7 | H7i 8 (57.1\%) |
|  |  | H14 | $\begin{gathered} \hline \text { H14b } 34 \\ (50.0 \%) \\ \hline \end{gathered}$ |
|  |  | H41 15 (78.9\%) | H41a 15 (78.9\%) |
|  |  | H55 26 <br> (76.5\%) | $\begin{gathered} \hline \text { H55b } 26 \\ (76.5 \%) \end{gathered}$ |
|  |  | $\begin{aligned} & \mathrm{H} 5788 \\ & (59.1 \%) \\ & \hline \end{aligned}$ | $\begin{aligned} & \mathrm{H} 5788 \\ & (59.1 \%) \\ & \hline \end{aligned}$ |
|  |  | H66 20 (76.9\%) | $\begin{gathered} \hline \text { H66a } 20 \\ (76.9 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{gathered} \hline \text { H101 } 29 \\ (82.9 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \mathrm{H} 10129 \\ (82.9 \%) \\ \hline \end{gathered}$ |



|  |  | B5 | $\begin{aligned} & \text { B5b 78 } \\ & (50.6 \%) \end{aligned}$ |
| :---: | :---: | :---: | :---: |
|  | F | F1 | $\begin{aligned} & \text { F1b } 77 \\ & (55.4 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { F1e 17 } \\ & (56.7 \%) \end{aligned}$ |
|  |  | F3 | $\begin{aligned} & \text { F3a } 41 \\ & (59.4 \%) \end{aligned}$ |
|  | H | H1 | H1h 14 <br> (70.0\%) |
|  |  |  | $\begin{gathered} \text { H1j } 75 \\ (67.0 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { H1n } 53 \\ & (80.3 \%) \end{aligned}$ |
|  |  |  | $\begin{gathered} \text { H1r } 9 \\ (90.0 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { H1v } 10 \\ & (62.5 \%) \end{aligned}$ |
|  |  |  | $\begin{gathered} \mathrm{H} 1 \mathrm{z} 8 \\ (53.3 \%) \end{gathered}$ |
|  |  | $\begin{aligned} & \text { H2 } 457 \\ & (55.7 \%) \end{aligned}$ | $\begin{gathered} \mathrm{H} 2 \mathrm{a} 432 \\ (55.5 \%) \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { H2b } 19 \\ & (65.5 \%) \end{aligned}$ |
|  |  | H3 | $\begin{aligned} & \text { H3b } 46 \\ & (63.0 \%) \end{aligned}$ |
|  |  | H5 | H5b 55 <br> (71.4\%) |
|  |  | H6 240 | $\begin{gathered} \text { H6a } 214 \\ (66.0 \%) \\ \hline \end{gathered}$ |
|  |  | (63.7\%) | $\begin{aligned} & \text { H6b } 19 \\ & (70.4 \%) \end{aligned}$ |
|  |  | $\begin{aligned} & \text { H7 } 162 \\ & (50.8 \%) \end{aligned}$ | $\begin{aligned} & \text { H7a } 42 \\ & (76.4 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { H7c } 31 \\ & (64.6 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { H7e } 23 \\ & (95.8 \%) \\ & \hline \end{aligned}$ |
|  |  | $\begin{gathered} \text { H8 } 29 \\ (53.7 \%) \\ \hline \end{gathered}$ | $\begin{aligned} & \mathrm{H} 8 \mathrm{c} 14 \\ & (60.9 \%) \end{aligned}$ |
|  |  | $\begin{gathered} \text { H10 } 116 \\ (75.8 \%) \end{gathered}$ | $\begin{aligned} & \text { H10a } 21 \\ & (72.4 \%) \end{aligned}$ |
|  |  |  | $\begin{gathered} \mathrm{H} 10 \mathrm{e} 53 \\ (84.1 \%) \\ \hline \end{gathered}$ |
|  |  | H11 | $\begin{aligned} & \text { H11b } 8 \\ & (61.5 \%) \end{aligned}$ |
|  |  | $\begin{gathered} \hline \text { H13 } 203 \\ (64.4 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \text { H13a } 182 \\ (65.7 \%) \\ \hline \end{gathered}$ |



|  |  | $\begin{aligned} & \mathrm{H} 1017 \\ & (50.0 \%) \end{aligned}$ | $\begin{aligned} & \mathrm{H} 1017 \\ & (50.0 \%) \end{aligned}$ |
| :---: | :---: | :---: | :---: |
|  | $\begin{aligned} & \text { HV } 442 \\ & (57.0 \%) \end{aligned}$ | HV0 | $\begin{aligned} & \text { HV0d } 9 \\ & (69.2 \%) \end{aligned}$ |
|  |  | $\begin{aligned} & \text { HV1 } 81 \\ & (60.9 \%) \end{aligned}$ | $\begin{gathered} \hline \text { HV1a } 48 \\ (64.0 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{gathered} \hline \text { HV1b } 30 \\ (60.0 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{aligned} & \text { HV2 } 25 \\ & (55.6 \%) \\ & \hline \end{aligned}$ | $\begin{gathered} \hline \text { HV2a } 21 \\ (56.8 \%) \\ \hline \end{gathered}$ |
|  |  | HV4 76 <br> (79.2\%) | $\begin{gathered} \hline \text { HV4 } 9 \\ (52.9 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{gathered} \hline \text { HV4a } 60 \\ (85.7 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{aligned} & \text { HV6 } 12 \\ & (66.7 \%) \end{aligned}$ | $\begin{aligned} & \text { HV6 } 9 \\ & (60.0 \%) \end{aligned}$ |
|  |  | HV9 29 <br> (78.4\%) | $\begin{aligned} & \text { HV9 } 14 \\ & \text { (93.3\%) } \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { HV9a } 8 \\ & (66.7 \%) \end{aligned}$ |
|  |  | HV12 | $\begin{gathered} \hline \text { HV12a } 7 \\ (58.3 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{aligned} & \text { HV13 } 9 \\ & (64.3 \%) \end{aligned}$ |  |
|  |  | $\begin{gathered} \text { HV14 50 } \\ (87.7 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \text { HV14a } 49 \\ (89.1 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{gathered} \text { HV16 } 13 \\ (86.7 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \text { HV16 } 13 \\ (86.7 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{gathered} \hline \text { HV18 } 10 \\ (76.9 \%) \\ \hline \end{gathered}$ | HV18 10 <br> (76.9\%) |
|  | I | I | I 14 (51.9\%) |
|  |  | I1 | $\begin{gathered} \text { I1 14 } \\ (66.7 \%) \end{gathered}$ |
|  |  |  | $\begin{gathered} \text { I1b } 20 \\ (54.1 \%) \end{gathered}$ |
|  |  |  | I1c 8 (57.1\%) |
|  |  |  | $\begin{gathered} \text { I1f } 15 \\ (71.4 \%) \end{gathered}$ |
|  |  | $\begin{gathered} \text { I2 } 93 \\ (55.4 \%) \end{gathered}$ | $\begin{gathered} \text { I2 } 56 \\ (56.0 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{gathered} \hline \text { I2a 18 } \\ (69.2 \%) \end{gathered}$ |
|  |  |  | I2d 16 (76.2\%) |
|  |  | $\begin{gathered} \text { I3 } 49 \\ \text { (75.4\%) } \end{gathered}$ | $\begin{gathered} \text { I3a } 28 \\ (77.8 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{gathered} \text { I3d } 10 \\ (83.3 \%) \\ \hline \end{gathered}$ |


|  |  | I4 | $\begin{gathered} \text { I4b } 6 \\ (54.5 \%) \\ \hline \end{gathered}$ |
| :---: | :---: | :---: | :---: |
|  | K | K1 | $\begin{gathered} \hline \text { K1b } 100 \\ (56.2 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{gathered} \text { K1d } 8 \\ (66.7 \%) \\ \hline \end{gathered}$ |
|  | N | $\begin{gathered} \text { N2 } 7 \\ (63.6 \%) \end{gathered}$ | $\begin{gathered} \hline \text { N2a } 7 \\ (63.6 \%) \end{gathered}$ |
|  |  | $\begin{gathered} \text { N7 9 } \\ (64.3 \%) \end{gathered}$ |  |
|  |  | $\begin{aligned} & \text { N9 } 205 \\ & \text { (63.1\%) } \end{aligned}$ | $\begin{gathered} \hline \text { N9a } 180 \\ (63.8 \%) \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { N9b 25 } \\ & (58.1 \%) \end{aligned}$ |
|  |  | N10 | $\begin{aligned} & \text { N10a } 7 \\ & (50.0 \%) \end{aligned}$ |
|  |  | N21 | $\begin{aligned} & \text { N21a } 6 \\ & (54.5 \%) \end{aligned}$ |
|  | P | $\begin{gathered} \text { P9 9 } \\ (81.8 \%) \end{gathered}$ |  |
|  | R | $\begin{aligned} & \text { R0 170 } \\ & (56.5 \%) \end{aligned}$ | $\begin{aligned} & \text { R0a } 151 \\ & (58.8 \%) \\ & \hline \end{aligned}$ |
|  |  | $\begin{gathered} \text { R1 } 43 \\ (60.6 \%) \end{gathered}$ | $\begin{aligned} & \text { R1a } 36 \\ & (73.5 \%) \\ & \hline \end{aligned}$ |
|  |  | $\begin{gathered} \text { R2 } 38 \\ (55.9 \%) \end{gathered}$ | $\begin{gathered} \hline \text { R2 14 } \\ (51.9 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { R2b } 12 \\ & (92.3 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { R2d } 10 \\ & (58.8 \%) \end{aligned}$ |
|  |  | $\begin{gathered} \text { R8 70 } \\ (69.3 \%) \end{gathered}$ | $\begin{aligned} & \text { R8a } 28 \\ & (52.8 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { R8b } 42 \\ & (87.5 \%) \end{aligned}$ |
|  |  | R9 | $\begin{aligned} & \text { R9b } 68 \\ & (50.4 \%) \\ & \hline \end{aligned}$ |
|  |  | R11 | $\begin{aligned} & \text { R11b } 9 \\ & (75.0 \%) \\ & \hline \end{aligned}$ |
|  |  | $\begin{gathered} \text { R21 } 6 \\ (50.0 \%) \end{gathered}$ | $\begin{gathered} \hline \text { R21 6 } \\ (50.0 \%) \\ \hline \end{gathered}$ |
|  |  | R30 | $\begin{aligned} & \hline \text { R30a } 26 \\ & (53.1 \%) \\ & \hline \end{aligned}$ |
|  | T | $\begin{aligned} & \text { T1 342 } \\ & (55.8 \%) \end{aligned}$ | $\begin{aligned} & \hline \text { T1a 310 } \\ & (55.2 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { T1b } 29 \\ & (72.5 \%) \end{aligned}$ |
|  |  | T2 | $\begin{gathered} \hline \text { T2 44 } \\ (51.8 \%) \\ \hline \end{gathered}$ |


| $\begin{aligned} & \text { ò } \\ & 0 \\ & 0 \\ & \text { ò } \\ & \text { ò } \end{aligned}$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $$ |  | $\begin{aligned} & \text { o્ } \\ & 0 \\ & 0 \\ & 0 \\ & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & \text { ふ } \\ & \text { O } \\ & \text { N } \end{aligned}$ |  |  |  |  |  |  |  |  |  | $\begin{aligned} & \text { Oc c } \\ & \text { ol } \\ & \text { de } \\ & \text { oc } \end{aligned}$ |  | $\begin{aligned} & \underset{N}{c} \\ & \text { N } \\ & =0.0 \end{aligned}$ |  | $\stackrel{\square}{\ddagger}$ |  |  |  |  |
|  |  | $\begin{array}{ll} \hline 0 & \leq \\ 0 & \omega \\ 0 & 0 \\ 0 & 0 \end{array}$ | $\left\lvert\,\right.$ |  |  |  |  |  | $\stackrel{3}{3}$ 6 6 0. 0. |  | $\begin{aligned} & < \\ & \infty \\ & \infty \\ & \stackrel{1}{n} \\ & \underset{\sim}{c} \\ & 0 \end{aligned}$ |  |  |  | $\begin{array}{cc} \text { Dr c } \\ \text { N } \\ 0 & 0 \\ 0 \\ 0 & 0 \end{array}$ |  |  |  |  |  |  |  |  |


|  |  | $\begin{aligned} & \text { V22 } 10 \\ & (83.3 \%) \end{aligned}$ | $\begin{aligned} & \text { V22 } 10 \\ & (83.3 \%) \end{aligned}$ |
| :---: | :---: | :---: | :---: |
|  | W | W1 | $\begin{aligned} & \text { W1a } 23 \\ & (53.5 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { W1b } 15 \\ & (57.7 \%) \end{aligned}$ |
|  |  | $\begin{gathered} \text { W3 } 83 \\ (60.1 \%) \end{gathered}$ | $\begin{aligned} & \text { W3a } 54 \\ & (58.7 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { W3b } 27 \\ & (62.8 \%) \end{aligned}$ |
|  |  | W5 | $\begin{aligned} & \text { W5a } 21 \\ & (56.8 \%) \\ & \hline \end{aligned}$ |
|  |  | $\begin{gathered} \text { W6 } 53 \\ (62.4 \%) \end{gathered}$ | $\begin{aligned} & \text { W6 } 24 \\ & (51.1 \%) \end{aligned}$ |
|  |  |  | W6a 14 <br> (70.0\%) |
|  | X | X2 | $\begin{aligned} & \text { X2a } 20 \\ & (55.6 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { X2e } 29 \\ & (67.4 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { X2i } 12 \\ & (70.6 \%) \end{aligned}$ |
|  |  |  | $\begin{gathered} \text { X2p } 7 \\ (70.0 \%) \end{gathered}$ |
|  |  | $\begin{gathered} \text { X3 6 } \\ (50.0 \%) \\ \hline \end{gathered}$ |  |
|  |  | $\begin{gathered} \text { X4 8 } \\ (80.0 \%) \end{gathered}$ | X4 8 (80.0\%) |
|  | $\begin{gathered} \text { Y } 70 \\ (50.4 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \text { Y2 } 29 \\ (53.7 \%) \end{gathered}$ | $\begin{gathered} \mathrm{Y} 2 \mathrm{a} 24 \\ (54.5 \%) \\ \hline \end{gathered}$ |

Supplementary Table S8-Analysis of m.16319G>A mtDNA variant frequency in haplogroups (number between brackets) using full length sequence set (left) or control region sequence set (right) deposited in MITOMAP database.

| Using Full Length sequence set |  |  |  |
| :---: | :---: | :---: | :---: |
| Lineage | Top Level HG | Top Level HG <br> Branch (ltr-num) | HG Branch (ltr-num-ltr) |
| $\begin{aligned} & \text { M } 939 \\ & (8.8 \%) \end{aligned}$ | D | $\begin{gathered} \hline \text { D339 } \\ (100.0 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \hline \text { D3 39 } \\ (100.0 \%) \\ \hline \end{gathered}$ |
|  | M | $\begin{aligned} & \text { M2 } 232 \\ & (95.1 \%) \end{aligned}$ | $\begin{gathered} \hline \text { M2a } 129 \\ (99.2 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { M2b } 96 \\ & (94.1 \%) \\ & \hline \end{aligned}$ |
|  |  | $\begin{gathered} \text { M8 88 } \\ (97.8 \%) \end{gathered}$ | $\begin{aligned} & \text { M8a } 87 \\ & (97.8 \%) \end{aligned}$ |
|  |  | $\begin{gathered} \text { M32 } 162 \\ (97.0 \%) \end{gathered}$ | $\begin{aligned} & \text { M32a } 10 \\ & (100.0 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{gathered} \hline \text { M32c } 152 \\ (99.3 \%) \\ \hline \end{gathered}$ |
|  |  | M35 | $\begin{gathered} \text { M35a } 14 \\ (50.0 \%) \end{gathered}$ |
|  |  | $\begin{aligned} & \hline \text { M40 } 19 \\ & (65.5 \%) \\ & \hline \end{aligned}$ | $\begin{gathered} \text { M40a } 19 \\ (67.9 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{gathered} \text { M467 } \\ (58.3 \%) \\ \hline \end{gathered}$ |  |
|  |  | $\begin{gathered} \hline \text { M55 13 } \\ (100.0 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \hline \text { M55 13 } \\ (100.0 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{gathered} \hline \text { M60 } \\ (64.3 \%) \end{gathered}$ | $\begin{aligned} & \text { M60a } 9 \\ & (90.0 \%) \end{aligned}$ |
| $\begin{aligned} & \text { N } 1810 \\ & (5.4 \%) \end{aligned}$ | $\begin{aligned} & \text { A } 1356 \\ & (97.2 \%) \end{aligned}$ | A | A 65 (98.5\%) |
|  |  | $\begin{gathered} \text { A1 13 } \\ (100.0 \%) \end{gathered}$ | $\begin{gathered} \hline \text { A1a 12 } \\ (100.0 \%) \end{gathered}$ |
|  |  | $\begin{aligned} & \text { A2 } 859 \\ & (96.0 \%) \end{aligned}$ | $\begin{aligned} & \text { A2 } 344 \\ & (97.2 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{aligned} & \hline \text { A2a } 225 \\ & (99.6 \%) \end{aligned}$ |
|  |  |  | $\begin{gathered} \hline \text { A2b } 43 \\ (100.0 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { A2d } 21 \\ & (84.0 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { A2f } 18 \\ & (94.7 \%) \\ & \hline \end{aligned}$ |


| Using Control Region sequence set |  |  |  |
| :---: | :---: | :---: | :---: |
| Lineage | Top Level HG | Top Level HG Branch (ltr-num) | HG Branch (ltr-num-ltr) |
| $\begin{gathered} \hline \text { L } 159 \\ (1.9 \%) \end{gathered}$ | L4 | L4 | L4 7 (58.3\%) |
| $\begin{gathered} \text { M } 1344 \\ (5.7 \%) \end{gathered}$ | M | $\begin{aligned} & \text { M2 } 124 \\ & (53.9 \%) \end{aligned}$ | $\begin{gathered} \hline \text { M2a } 110 \\ (90.9 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { M2b } 14 \\ & (66.7 \%) \end{aligned}$ |
|  |  | $\begin{aligned} & \text { M8 435 } \\ & (75.5 \%) \end{aligned}$ | $\begin{gathered} \hline \text { M8a } 435 \\ (99.1 \%) \end{gathered}$ |
|  |  | M12 | $\begin{gathered} \text { M12b } 82 \\ (59.0 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{aligned} & \hline \text { M32 50 } \\ & (98.0 \%) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline \text { M32c } 48 \\ & (100.0 \%) \\ & \hline \end{aligned}$ |
|  |  | M40 | $\begin{aligned} & \text { M40a } 8 \\ & (50.0 \%) \end{aligned}$ |
|  |  | $\begin{gathered} \text { M55 } 22 \\ (100.0 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \text { M55 } 22 \\ (100.0 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{aligned} & \hline \text { M60 13 } \\ & (54.2 \%) \end{aligned}$ | $\begin{gathered} \hline \text { M60a } 13 \\ (81.2 \%) \\ \hline \end{gathered}$ |
| $\begin{aligned} & \text { N } 4381 \\ & (10.6 \%) \end{aligned}$ | $\begin{aligned} & \text { A } 3718 \\ & (98.6 \%) \end{aligned}$ | A | $\begin{gathered} \text { A 916 } \\ (97.7 \%) \end{gathered}$ |
|  |  | $\begin{gathered} \text { A1 } 29 \\ (100.0 \%) \\ \hline \end{gathered}$ | $\begin{gathered} \text { A1a } 29 \\ (100.0 \%) \\ \hline \end{gathered}$ |
|  |  | $\begin{aligned} & \text { A2 } 1570 \\ & (98.6 \%) \end{aligned}$ | $\begin{aligned} & \hline \text { A2 } 797 \\ & (98.8 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{aligned} & \hline \text { A2a } 332 \\ & (98.2 \%) \end{aligned}$ |
|  |  |  | $\begin{aligned} & \hline \text { A2b } 222 \\ & (100.0 \%) \end{aligned}$ |
|  |  |  | $\begin{gathered} \hline \text { A2d 98 } \\ (100.0 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{gathered} \hline \text { A2g } 14 \\ (100.0 \%) \\ \hline \end{gathered}$ |
|  |  |  | $\begin{aligned} & \text { A2m } 18 \\ & (100.0 \%) \\ & \hline \end{aligned}$ |
|  |  |  | $\begin{gathered} \text { A2q } 19 \\ (100.0 \%) \\ \hline \end{gathered}$ |



|  | B | B2 | B2y 8 <br> $(57.1 \%)$ |
| :---: | :---: | :---: | :---: |
|  | H | H31 | H31a 12 <br> $(92.3 \%)$ |
|  | I | I 1 | I1c 12 <br> $(85.7 \%)$ |
|  | N | N2 11 <br> $(100.0 \%)$ | N2a 11 <br> $(100.0 \%)$ |
|  | R | R7 28 <br> $(100.0 \%)$ | R7a 16 <br> $(100.0 \%)$ |

