**Supplementary figures**

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**Figure S1. ADL score of the participants in this study.**

463 participants were involved in this study. 218 participants were healthy controls, and 245 participants were disability cases.



**Figure S2. Morphometric analysis of M7 cybrids and M8 cybrids.**

Morphology of M8 and M7 cybrids in their best growth conditions. The scale bar is 200 µm.



**Figure S3. Kaplan-Meier survival analysis of M7 and non-M7 haplogroup groups.**

Kaplan–Meier survival analysis shows the survival rate of the M7 haplogroup group and non-M7 haplogroup groups after a six-year follow-up. LogRank =0.188.

**Table S1 Distribution of basic indicators in different disability groups**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Normal | Disability | All | p-value |
|  | (n = 218) | (n = 245) | (n = 463) |  |
| Age | 97.25 ± 2.02 | 97.58 ± 2.16 | 97.42 ± 2.10 | 0.095 |
| Gender (%) |  |  |  | 0.098 |
|  Male | 55 (25.2%) | 48 (19.5%) | 103 (22.2%) |  |
|  Female | 163 (74.8%) | 197 (80.5%) | 360 (77.8%) |  |
| Marriage status |  |  |  | 0.875 |
|  Married | 12 (5.5%) | 11 (4.5%) | 23 (5.0%) |  |
|  Widowed | 204 (93.6%) | 232 (94.7%) | 436 (94.2%) |  |
|  Unmarried | 2 (0.9%) | 2 (0.8%) | 4 (0.9%) |  |
| Smoking habits |  |  |  | 0.292 |
|  Smoked | 20 (9.2%) | 18 (7.3%) | 38 (8.2%) |  |
|  Never smoked | 198 (90.8%) | 227 (92.7%) | 425 (91.8%) |  |
| Drinking habits |  |  |  | 0.213 |
|  Drink | 78 (35.8%) | 78 (31.8%) | 156 (33.7%) |  |
|  Never  | 140 (64.2%0 | 167 (68.2%0 | 307 (66.3%) |  |
| Height (cm) | 153.47 ± 10.16 | 153.63 ± 11.78 | 153.55 ± 11.03 | 0.873 |
| Weight (kg) | 52.01 ± 10.88 | 50.40 ± 11.53 | 51.17 ± 11.24 | 0.125 |
| BMI (kg/m2) | 21.91 ± 4.19 | 21.18 ± 4.12 | 21.53 ± 4.17 | 0.062 |
| SBP (mmHg) | 138.93 ± 22.62 | 134.72 ± 22.52 | 136.71 ± 22.64 | 0.046 |
| DBP (mmHg) | 80.48 ± 11.05 | 79.59 ± 10.99 | 80.01 ± 11.02 | 0.382 |
| Hypertension | 111 (50.9%) | 101 (41.2%) | 212 (45.8%) | 0.023 |
| GLU (mmol/L) | 4.87 ± 1.23 | 5.01 ± 1.40 | 4.95 ± 1.32 | 0.381 |
| ADL | 6.00 ± 0.00 | 11.06 ± 3.62 | 8.33 ± 3.66 | <0.001 |
| IADL | 10.15 ± 3.00 | 14.55 ± 2.80 | 12.47 ± 3.64 | <0.001 |
| Hemoglobin (g/L) | 128.44 ± 19.42 | 128.47 ± 20.68 | 128.45 ± 20.09 | 0.987 |
| Platelets (10^9/L) | 158.65 ± 59.16 | 172.16 ± 73.94 | 165.87 ± 67.73 | 0.035 |
| White blood cell (10^9/L) | 5.40 ± 1.60 | 5.44 ± 1.74 | 5.42 ± 1.67 | 0.79 |
| Albumin (g/L) | 43.10 ± 4.23 | 41.56 ± 8.86 | 42.27 ± 4.64 | <0.001 |
| Protein (g/L) | 70.61 ± 6.54 | 69.74 ± 6.55 | 70.15 ± 6.55 | 0.159 |
| Phosphatase (IU/L) | 82.65 ± 23.23 | 89.40 ± 27.59 | 86.26 ± 25.85 | 0.006 |
| Creatinine (µmol/L) | 67.92 ± 20.33 | 63.34 ± 19.36 | 65.43 ± 19.91 | 0.052 |
| UA (µmol/L) | 286.97 ± 94.05 | 276.78 ± 92.83 | 281.55 ± 93.97 | 0.253 |
| CHOL (mmol/L) | 4.79 ± 0.95 | 4.77 ± 0.96 | 4.78 ± 0.96 | 0.813 |
| TG (mmol/L) | 1.07 ± 0.47 | 1.12 ± 0.52 | 1.10 ± 0.50 | 0.273 |
| LDL (mmol/L) | 2.50 ± 0.70 | 2.49 ± 0.68 | 2.50 ± 0.69 | 0.923 |
| HDL (mmol/L) | 1.40 ± 0.33 | 1.35 ± 0.34 | 1.37 ± 0.34 | 0.152 |
| Status of survival (%) |  |  |  | 0.003 |
|  Survival | 29 (13.4%) | 13 (5.5%) | 42 (9.3%) |  |
|  Death | 187 (86.6%) | 223 (94.5%) | 410 (90.7%) |  |

Values in parentheses are the percentage of samples. BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; GLU: glucose in urine; UA: uric acid; CHOL: cholesterol; TG: triglyceride; LDL: low density lipoprotein; HDL: high density lipoprotein. P-value: Chi-square test was used in the table.

**Table S2 Multivariate regression analysis of mtDNA haplogroup M7 and disability**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Model 1 | Model 2 | Model 3 |
|  |  OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Non-M7 | Ref | ref | ref |
| M7 | 3.28 (1.46 - 7.39) | 3.20 (1.42 - 7.22) | 3.18 (1.29 - 7.83) |
| p-value | 0.004 | 0.005 | 0.012 |

CI, confidence interval; OR, odds ratio.

Model 1: Crude model;

Model 2: Age, Sex;

Model 3: Age, Sex, Marriage, Smoking habits, Drinking habits, Hemoglobin, BMI, SBP, DBP, Platelets, White blood cell, Albumin, Phosphatase, UA, CHOL, TG, LDL, HDL.

**Table S3 Decision mtSNPs for haplogroup assignment**

|  |  |
| --- | --- |
|  |  |
| Haplogroup | Key multiplex SNP variants |
| A | 1736G 10873T |
| B | 9bp- deletion 10873T |
| B4 | T16217C 9bp- deletion 10873T |
| B5 | 8584A 9bp- deletion 10873T |
| D | 5178A 10400T |
| D4 | 3010A 5178A 10400T |
| D5 | 1107C 5178A 10400T |
| F | 3970T 12705C 10873T |
| F1 | 12406A 3970T 12705C 10873T |
| G | 4833G 14569A 10400T |
| G2 | 7600A 4833G 14569A 10400T |
| M7 | 6455T 9824C 10400T |
| M8 | 7196A 10400T |
| M9 | 4491A 3705G 10400T |
| M10 | 10646A 10400T |
| M12 | 14569A 10400T |
| N9 | 5417A 10873T |

**Table S4 Analysis of whole mitochondrial genome**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| position | Gene | rCRS base | mutation | AA change | mtDNA database\*\* |
| M8-1 | M8-2 | M7-1 | M7-2 |
| 73 | D-loop | A | G | G | G | G | no | polymorphic site |
| 150 | D-loop | C |  |  | T | T | no | polymorphic site |
| 152 | D-loop | T | C |  |  |  | no | polymorphic site |
| 199 | D-loop | T |  |  | C | C | no | polymorphic site |
| 204 | D-loop | T |  |  | C | C | no | polymorphic site |
| 263 | D-loop | A | G | G | G | G | no | polymorphic site |
| 489 | D-loop | T | C | C | C | C | no | polymorphic site |
| 509 | D-loop | C |  |  | T |  | no | polymorphic site |
| 750 | 12S rRNA | A | G | G | G | G | no | polymorphic site |
| 1438 | 12S rRNA | A | G | G | G | G | no | polymorphic site |
| 2706 | 16S rRNA | A | G | G | G | G | no | polymorphic site |
| 2835 | 16S rRNA | C |  | T |  |  | no | polymorphic site |
| 3483 | ND1 | G |  |  |  | A | no | polymorphic site |
| 4048 | ND1 | G |  |  | A | A | Asp > Asn | polymorphic site |
| 4071 | ND1 | C |  |  | T | T | no | polymorphic site |
| 4164 | ND1 | A |  |  | G | G | no | polymorphic site |
| 4670 | ND2 | C |  | T |  |  | no | polymorphic site |
| 4715 | ND2 | A | G | G |  |  | no | polymorphic site |
| 4769 | ND2 | A | G | G | G | G | no | polymorphic site |
| 4841 | ND2 | G | A |  |  |  | no | polymorphic site |
| 5100 | ND2 | C | T |  |  |  | no | polymorphic site |
| 5261 | ND2 | G |  |  | A |  | no | polymorphic site |
| 5351 | ND2 | A |  |  | G | G | no | polymorphic site |
| 5460 | ND2 | G |  |  | A | A | Ala > Thr | polymorphic site |
| 6179 | COI | G | A | A |  |  | no | polymorphic site |
| 6455 | COI | C |  |  | T | T | no | polymorphic site |
| 6671 | COI | T |  | C |  |  | no | polymorphic site |
| 6680 | COI | T |  |  | C | C | no | polymorphic site |
| 7028 | COI | C | T | T | T | T | no | polymorphic site |
| 7196 | COI | C | A | A |  |  | no | polymorphic site |
| 7598 | COII | G |  |  |  | A | Ala > Thr | polymorphic site |
| 7684 | COII | T |  |  | C | C | no | polymorphic site |
| 7853 | COII | G |  |  | A | A | Val > Ile | polymorphic site |
| 8572 | ATPase8 | G |  |  |  | A | no | polymorphic site |
| 8584 | ATPase6 | G | A | A |  |  | Ala > Thr | polymorphic site |
| 8684 | ATPase6 | C | T | T |  |  | Thr > Ile | polymorphic site |
| 8701 | ATPase6 | A | G | G | G | G | Thr > Ala | polymorphic site |
| 8860 | ATPase6 | A | G | G | G | G | Thr > Ala | polymorphic site |
| 9540 | COIII | T | C | C | C | C | no | polymorphic site |
| 9548 | COIII | G | A |  |  |  | no | polymorphic site |
| 9824 | COIII | T |  |  | C | C | no | polymorphic site |
| 10398 | ND3 | A | G | G | G | G | Thr > Ala | polymorphic site |
| 10400 | ND3 | C | T | T | T | T | no | polymorphic site |
| 10873 | ND4 | T | C | C | C | C | no | polymorphic site |
| 11255 | ND4 | T |  | C |  |  | Tyr > His | polymorphic site |
| 11719 | ND4 | G | A | A | A | A | no | polymorphic site |
| 12405 | ND5 | C |  |  | T | T | no | polymorphic site |
| 12705 | ND5 | C | T | T | T | T | no | polymorphic site |
| 12811 | ND5 | T |  |  | C | C | Tyr > His | polymorphic site |
| 13050 | ND5 | A |  | G |  |  | no | polymorphic site |
| 13401 | ND5 | T |  |  | C |  | no | polymorphic site |
| 13488 | ND5 | T | C |  |  |  | no | polymorphic site |
| 14256 | ND6 | T |  |  | C |  | no | no |
| 14470 | ND6 | T | C | C |  |  | no | polymorphic site |
| 14766 | Cytb | C | T | T | T | T | Thr > Ile | polymorphic site |
| 14783 | Cytb | T | C | C | C | C | no | polymorphic site |
| 14893 | Cytb | A |  |  |  | G | no | polymorphic site |
| 15043 | Cytb | G | A | A | A | A | no | polymorphic site |
| 15301 | Cytb | G | A | A | A | A | no | polymorphic site |
| 15326 | Cytb | A | G | G | G | G | Thr > Ala | polymorphic site |
| 15487 | Cytb | A | T | T |  |  | no | polymorphic site |
| 16129 | D-loop | G |  |  | A |  | no | polymorphic site |
| 16153 | D-loop | G |  | A |  |  | no | polymorphic site |
| 16184 | D-loop | C | T | T |  |  | no | polymorphic site |
| 16192 | D-loop | C |  |  | T |  | no | polymorphic site |
| 16223 | D-loop | C | T | T | T | T | no | polymorphic site |
| 16245 | D-loop | C | T |  |  |  | no | polymorphic site |
| 16278 | D-loop | C |  |  |  | T | no | polymorphic site |
| 16291 | D-loop | C |  |  | T |  | no | polymorphic site |
| 16293 | D-loop | A | G |  |  |  | no | polymorphic site |
| 16297 | D-loop | T |  |  | C | C | no | polymorphic site |
| 16298 | D-loop | T | C | C |  |  | no | polymorphic site |
| 16319 | D-loop | G | A | A |  |  | no | polymorphic site |
| 16519 | D-loop | T |  |  | C |  | no | polymorphic site |
| rCRS: revised Cambridge Reference Sequence |  |  |  |  |
| AA: Amino Acid |  |  |  |  |  |  |  |
| \*\* databases: MITOMAP, mtDB, mtSNP and PhyloTree mt |  |  |  |  |