Mitochondrial DNA variants in inclusion body myositis

characterized by deep sequencing

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Supplementary material
Supplementary Figure 1. Circular maps of deletions (blue) and duplications (red) identified in all the control and IBM muscle samples at 0.05% heteroplasmy cut-off for visualization. The color intensity is related to the abundance of each rearrangement.
Supplementary Table 1. Variants identified in selected nuclear genes. These twelve genes are known to be associated with diseases with multiple mtDNA deletions in muscle.

| Gene   | Transcript | Protein | Translation | gnomAD | Total number of variants |
|--------|------------|---------|-------------|--------|-------------------------|
| RNASEH1|            |         |             |        |                         |
| Symbol |            | Variant | Impact      | Frequency | Homozygous |
|        | c.498A>G   | p.P166P | synonymous  | 33.462   | 17460       |
|        |            |         |             | 8        | 13          |
|        | c.420G>T   | p.V140V | synonymous  | 0.809    | 22          |
|        | c.473G>A   | p.S158N | missense    | 47.320   | 31626       |
|        | c.2109T>C  | p.A703A | synonymous  | 47.224   | 31536       |
|        | c.2808G>A  | p.A936A | synonymous  | 0.935    | 104         |
|        | c.207C>T   | p.V69V  | synonymous  | 2.937    | 175         |
| DNA2   |            |         |             |          |             |
|        | c.1971G>A  | p.T657T | synonymous  | 4.422    | 418         |
|        | c.507C>A   | p.A169A | synonymous  | 0.935    | 16          |
|        | c.2109T>C  | p.A703A | synonymous  | 0.935    | 104         |
|        | c.2808G>A  | p.A936A | synonymous  | 0.935    | 104         |
| TWNK   |            |         |             |          |             |
|        | c.639C>T   | p.G213G | synonymous  | 0.115    | 1           |
|        | c.1102G>A  | p.V368I | missense    | 2.462    | 227         |
|        | c.1572C>T  | p.H524H | synonymous  | 0.004    | 0           |
| POLG   |            |         |             |          |             |
|        | c.3708G>T  | p.Q1236H| missense    | 6.275    | 808         |
|        | c.597G>A   | p.T1199T| synonymous  | 0.777    | 16          |
|        | c.3198G>A  | p.T1066T| synonymous  | 0.584    | 10          |
|        | c.2492A>G  | p.Y831C | missense    | 0.701    | 18          |
|        | c.581C>T   | p.A194V | missense    | 0.001    | 0           |
|        | c.153_158del| p.Q54,Q55dup| in-frame  | 3.646    | 9           |
|        | c.150_158del| p.Q53,Q55del| in-frame  | 0.183    | 18          |
| TK2    |            |         |             |          |             |
|        | c.94C>T    | p.R32W  | missense    | 0.785    | 2           |
| SPG7   |            |         |             |          |             |
|        | c.120G>A   | p.G40G  | synonymous  | 0.930    | 15          |
|        | c.1507G>A  | p.T503A | missense    | 14.600   | 3498        |
|        | c.2063G>A  | p.R688Q | missense    | 14.496   | 3418        |
|        | c.2280G>A  | p.P760P | synonymous  | 1.270    | 26          |
|        | c.2292C>T  | p.I764I | synonymous  | 2.838    | 158         |
| POLG2  |            |         |             |          |             |
|        | c.1296C>T  | p.S423S | synonymous  | 7.391    | 945         |
|        | c.1247G>C  | p.G416A | missense    | 1.044    | 26          |
|        | c.1158T>G  | p.D386E | missense    | 0.638    | 73          |
|        | c.505G>A   | p.A169T | missense    | 16.411   | 8154        |
| TYMP   |            |         |             |          |             |
|        | c.1412C>T  | p.S471L | missense    | 12.355   | 2528        |
|        | c.1393G>A  | p.A465T | missense    | 4.521    | 369         |
|        | c.1284T>A  | p.G428G | synonymous  | 11.656   | 860         |
|        | c.972C>T   | p.A324A | synonymous  | 58.955   | 23242       |
| MPV17  |            |         |             |          |             |
|        | No variants|         |             |          |             |
| SLC25A4|            |         |             |          |             |
|        | No variants|         |             |          |             |

n: Number of investigated muscle samples

RNASEH1: NM_002936.4, OPA1: NM_015560.2, RRM2B: NM_015713.4, TWNK: NM_002830.4, POLG: NM_002693.2, TK2: NM_004614.4, SPG7: NM_003119.3, POLG2: NM_007215.3, TYMP: NM_000953.3, MPV17: NM_002437.4, SLC25A4: NM_001151.3