Figure e-1. (A) Comparison of total mtDNA content in blood leukocytes from British and German controls. There was no statistically significant difference between these two control groups (British controls: mean = 56.9, SD = 43.3, n = 87; German controls: mean = 68.7, SD = 39.4, n = 44, NS at P value = 0.1306), (B) Total mtDNA content in blood leukocytes from Danish OPA1+ve patients (Mean = 314.2, SD = 185.8, n = 49) compared with the merged British and German control dataset (Mean = 60.9, SD = 42.3, n = 131). *** refers to a P value < 0.0001.
Figure e-2. (A) OPA1 mutational subgroup analysis (Missense mutations: mean = 126.8, SD = 62.6, n = 31; other mutational subtypes: mean = 216.1, SD = 208.2, n = 119, NS with Bonferroni correction at P value = 0.0199), (B) OPA1 functional gene domain analysis (GTPase region: mean = 219.8, SD = 202.6, n = 60; other gene domains: mean = 164.0, SD = 94.0, n = 90, NS with Bonferroni correction at P value = 0.0244). *** refers to a P value < 0.0001. NS refers to a non-significant P value, with P < 0.0167 being the level of statistical significance after Bonferroni correction for multiple testing.
Method e-1

Methods used to extract DNA from the blood leukocyte fraction of venous blood: (A)
British cohort: Nucleon DNA extraction kit (Tepnel Lifescience, Manchester, UK), (B)
Danish cohort: Chemagic Magnetic Separation Module I (Chemagen, Baesweiler, Germany), (C) German cohort: Flexi-Gene kit (Qiagen, Hilden, Germany).
Method e-2

For the purpose of statistical analysis, Snellen visual acuity ratios were converted to LogMAR (Logarithm of the minimum angle of resolution) decimal values. A LogMAR value of 0 is equivalent to 20/20 Snellen vision and a value of 1.0 is equivalent to 20/200 Snellen vision, the largest optotype on standard Snellen charts. Patients with visual acuities reduced to counting fingers (CF) were assigned a LogMAR value of 2.0, whilst those with only hand movement (HM) perception were assigned a LogMAR value of 2.3.1-2 Visual acuity data was available for 51 OPAI+ve patients in the British cohort.
