SUPPLEMENTARY MATERIAL

Mitochondrial DNA mutation analysis from exome sequencing –a holistic approach in diagnostics of suspected mitochondrial disease

Matias Wagner, MD[1,2,3], Riccardo Berutti, PhD[1,2], Bettina Lorenz-Depiereux, PhD[2], Elisabeth Graf, PhD[2], Gertrud Eckstein, PhD[2], Johannes A. Mayr, PhD[4], Thomas Meitinger, MD[1,2], Uwe Ahting, PhD[1], Holger Prokisch, PhD[1,2], Tim M. Strom, MD[1,2], Saskia B. Wortmann, MD, PhD[1,2,4]

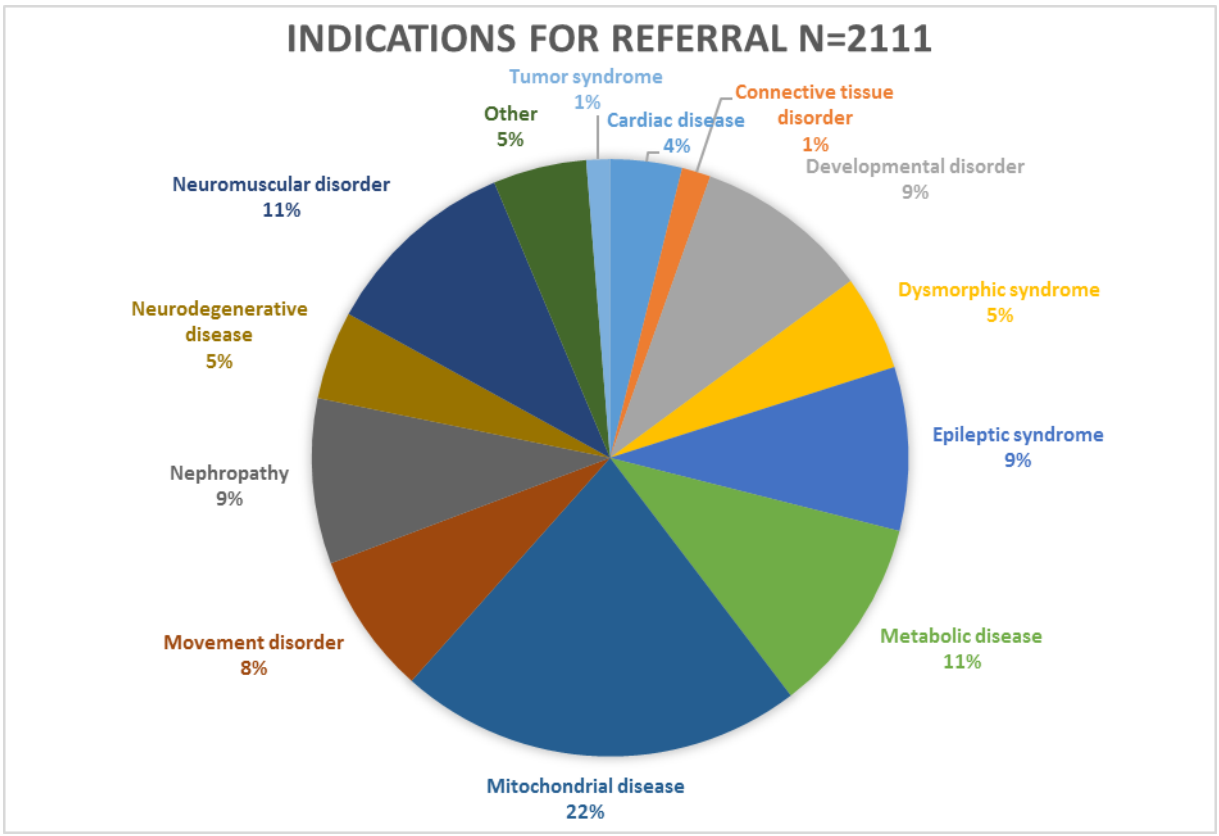
1. Institute of Human Genetics, Technical University München, Munich, Germany;
2. Institute of Human Genetics, Helmholtz Zentrum München, Neuherberg, Germany;
3. Institute for Neurogenomics, Helmholtz Zentrum München, Neuherberg, Germany
4. University Childrens Hospital, Paracelsus Medical University (PMU), Salzburg, Austria

Running title: mtDNA mutation analysis from exome sequencing

Corresponding author: Saskia B. Wortmann, MD, PhD. Institute of Human Genetics, Technical University Munich, Munich, Germany. T + 49-894140 8998, F +6382. wortmann-hagemann@helmholtz-muenchen.de

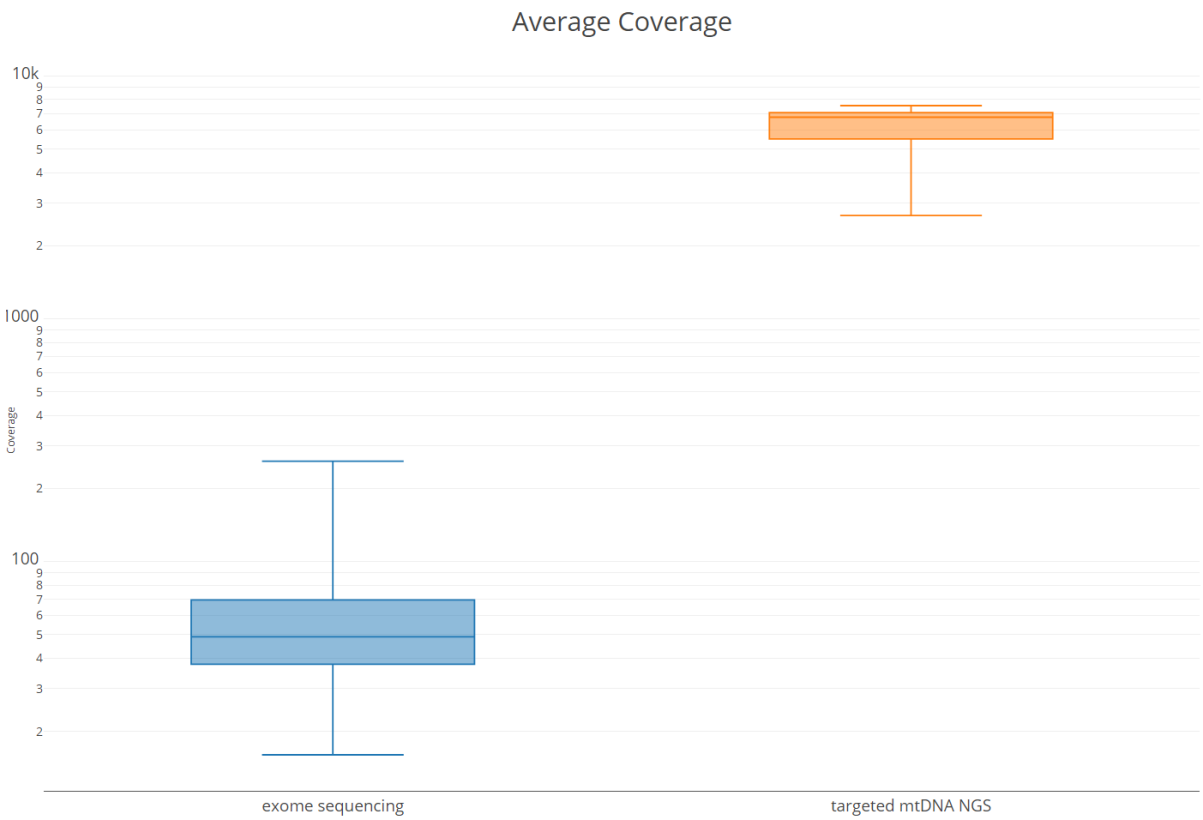
Supplementary Figures

Supplement figure 1:



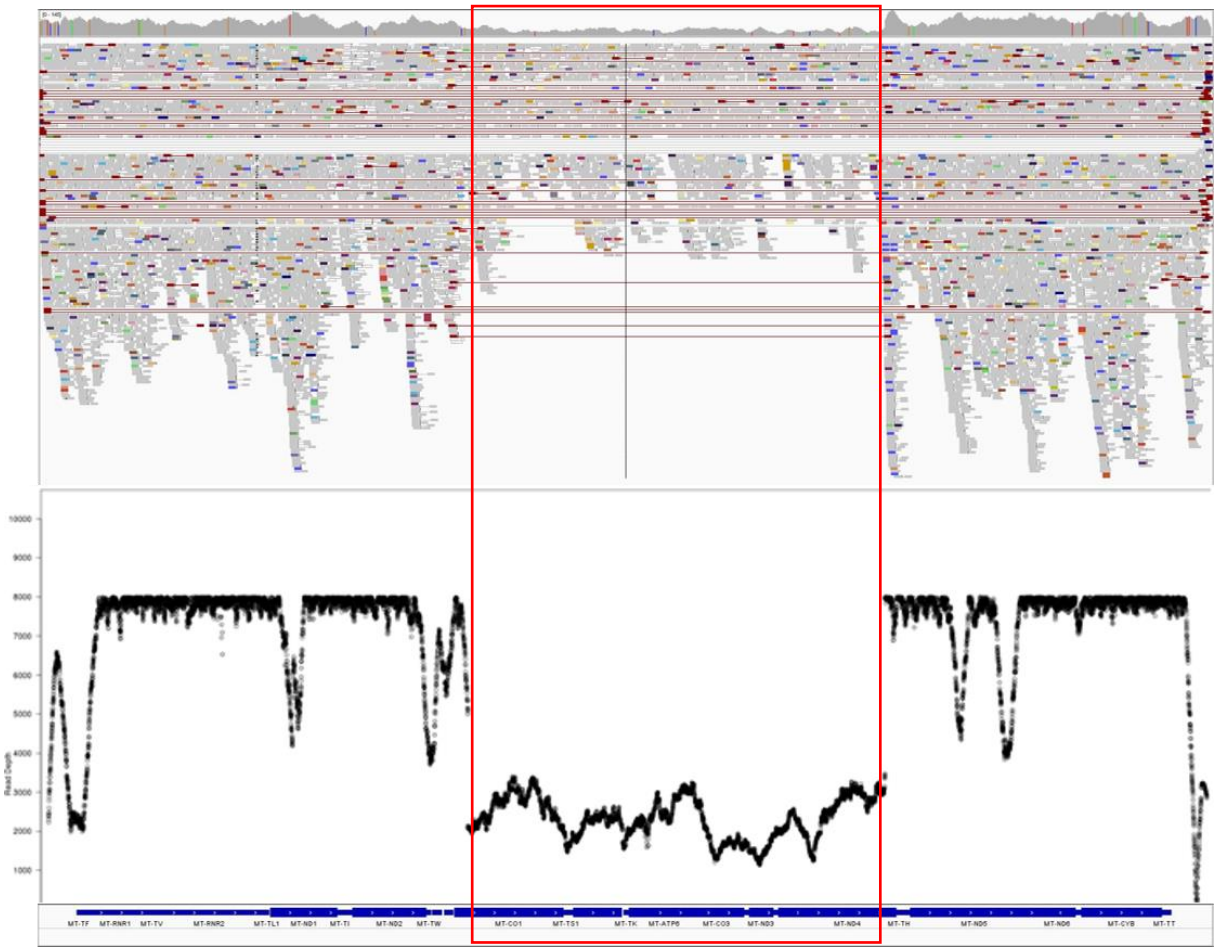
Supplement figure 1: Reasons for referral of 2,111 cases included in the study. The figure shows the reasons for referral of all cases that were included in the present study. A large proportion of cases were referred with neurometabolic disorders.

Supplement figure 2:



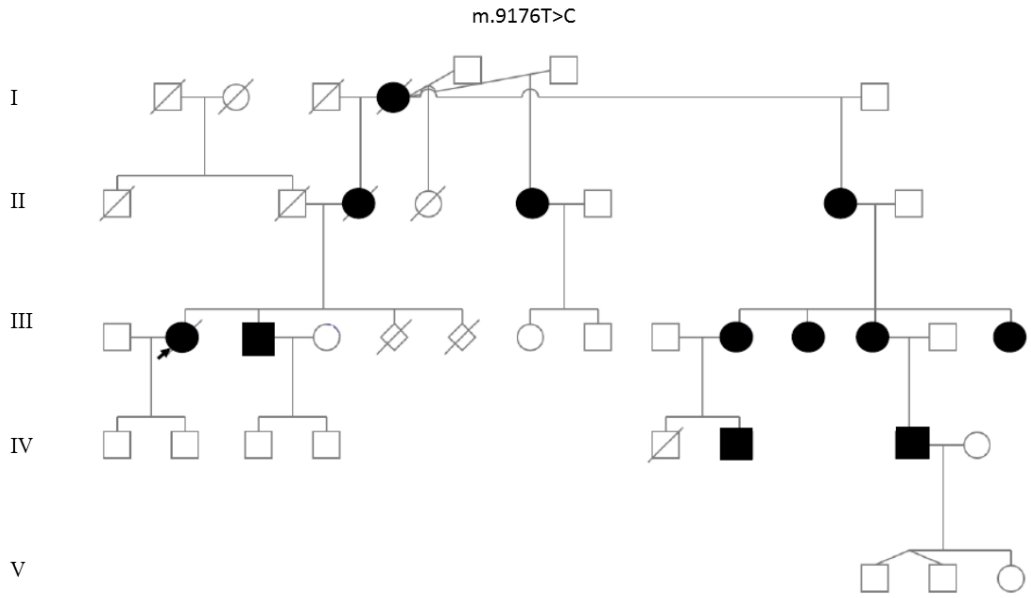
Supplement figure 2: Comparison of the average coverage of the mtDNA between ES and targeted mtDNA-NGS. The figure shows a comparison of the average coverage of 49 samples for which ES and targeted mtDNA-NGS was performed. The Y-axis is logarithmic scaled. MtDNA coverage by ES ranged from 16x to 259x (average 58±38x). Targeted mtDNA-NGS coverage was much higher ranging from 2665x to 7556x (average 6280±1107x)

Supplement figure 3



Supplement figure 3: Visualization of the 6kb deletion identified in individual 38. The figure shows alignment of exome sequencing reads to the revised Cambridge reference sequence using the integrative genomic viewer (middle panel). The deletion which is highlighted by a red rectangle leads to a dop in coverage (top panel). Split reads mark the deletion (middle panel). In comparison, the bottom panel shows a coverage plot of the mtDNA by targeted mtDNA-NGS.

Supplement figure 4



Supplement figure 4: Pedigree of the family of individual 23 in which Exome sequencing identified the mutation m.9176T>C. Exome sequencing was performed from brain DNA of the index patient indicated by an arrow. The variant was confirmed by Sanger sequencing in the affected brother of the index patient.