

Suppl. Figure S1: Fibroblast Respirometry in Subjects 6 and 9 help determine pathogenicity of variants. A. Respirometry in Subject 6 shows a very low oxygen consumption rate in response to substrates stimulating complex I (glutamate), complex II (succinate), complex III (duroquinol) and fatty acid oxidation (palmitoylcarnitine). Oxygen consumption is normalized by the addition of an uncoupler. This results in a high uncoupled ratio, supporting the hypothesis that complex V is ultimately the defective step and respiration normalizes once CI-IV are uncoupled from CV. B. Respirometry in Subject 9 shows normal oxygen consumption in response to all substrates and a normal uncoupled ratio. In combination with supportive *in silico* evaluation of the variant results in reclassifying this variant as likely benign.