



Figure S1 Expression of *NDI1* protein in *ND6d^{KO}* cells. (A) Immunodetection of *NDI1* (*NDI1HA*) using anti-HA antibody. The yeast enzyme was expressed and the protein apparently co-localized with mitochondria, revealed by staining with Mitotracker[®] Red (Invitrogen). (B) Allele-specific primer extension termination. The pool of galactose-resistant cells and all individual clones maintained homoplasmy for the deletion of cytosine 13887 in the *mt-Nd6* gene. (C) Polarographic measurements for wild-type cells (gray), complex I mutant (*ND6d^{KO}*) cells (red) and *NDI1* transformed *ND6d^{KO}* cells (green). Note the differences between the traces for wild-type, *ND6d^{KO}* and *ND6d^{KO}NDI1* cells. In the *ND6d^{KO}* cells NADH-linked substrate (glutamate+malate) oxygen consumption is undetectable, while the activities of CII+CIII (succinate+glycerol-3-P-linked oxygen consumption) and CIV (TMPD-linked oxygen consumption) are comparable to those of wild-type cells. Note that in *NDI1* transformed cells glutamate+malate driven respiration was insensitive to the complex I inhibitor rotenone, but sensitive to flavone, an inhibitor of *NDI1*, indicating that this respiration was due to the function of the yeast enzyme. G+M: glutamate+malate; Rot: rotenone; G3P+Succ: glycerol-3-P+succinate; AA: antimycin A; TMPD: N,N,N',N'-tetramethyl-p-phenyl-enediamine; KCN: potassium cyanide

1 ACCATGTCTGTCCTGACGCCACTGCTGCTGAGGAGCCTGACCGGCAGCGCCCGGGCGGCTC
61 ATGGTGCCCGGGCTCAGGTCATGAACAACACTACATCTTCGTGCTGAGCAGCCTGTTCCCTG
121 GTGGGCTGTCTGGGCCTGGCCCTGAAGCCAAGCCCAATCTACGGCGGCCTGGGCCTGATC
181 GTGAGCGGCTTCGTGGGCTGTCTGATGGTGCTGGGCTTCGGCGGCAGCTTCCTGGGCCTG
241 ATGGTGTTCCTGATCTACCTGGGCGGCATGCTGGTGGTGTTCGGCTACACAACAGCCATG
301 GCCACAGAGGAGTACCCAGAGACATGGGGCAGCAACTGGCTGATCCTGGGCTTCCTGGTG
361 CTGGGCGTGATCATGGAGGTGTTCCCTGATCTGTGTGCTGAACTACTACGATGAGGTGGGC
421 GTGATCAACCTGGATGGCCTGGGCGATTGGCTGATGTACGAGGTGGATGATGTGGGCGTG
481 ATGCTGGAGGGCGGCATCGGCGTGGCCGCCATGTACAGCTGTGCCACATGGATGATGGTG
541 GTGGCCGGCTGGAGCCTGTTCCGCGGCATCTTCATCATCATCGAGATCACAAGGGATTAA

Figure S2 *Allotopic expression gene*. Sequence of the nuclear encoded Nd6 gene, with the MTS of C8 (in blue), adapted to the mouse codon usage. The partial Kozac sequence is shown in red.