Supplementary Information

Supplementary Figure 1a, Full-length Western Blots (Figure 1d).

- **NCLX**
  - MCM x Slc8b1fl/fl
  - ~64 kD

- **MCU**
  - MCM x Slc8b1fl/fl
  - ~34 kD

- **MCUb**
  - MCM x Slc8b1fl/fl
  - ~35 kD

- **MICU1**
  - MCM x Slc8b1fl/fl
  - ~44 kD

- **EMRE**
  - MCM x Slc8b1fl/fl
  - ~11 kD

- **LETM1**
  - MCM x Slc8b1fl/fl
  - ~77 kD

- **VDAC**
  - MCM x Slc8b1fl/fl
  - ~30 kD

- **OxPhos Complexes**
  - CV-Sca, CIII-C2, CIV-S1, CIV-SDHB, CIV-SIV

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**SI Figure 1b, Band Density Results (Figure 1b).**

- NCLX Expression
- MCU Expression
- MICU1 Expression
- EMRE Expression
- VDAC Expression
- MCUb Expression
- LETM1 Expression

**SI Figure 1c, Full-length Western Blots (Ext. Data Figure 2b).**

- CYPD
- ANT
SI Figure 1d, Band Density Results (Ext. Data Figure 2k and 2n)

CYPD Expression

ANT Expression

p-PDH/Total PDH E1

SI Figure 1e, Full-length Western Blots (Extended Data Figure 3a)

NCLX

MCU

MCUb

MICU1

EMRE

LETM1

VDAC

OxPhos Complexes
SI Figure 1f, Band Density Results (Ext. Data Fig 3a).

**MCU Expression**
(Fold Change vs Con, CV-corrected)

**EMRE Expression**
(Fold Change vs Con, CV-corrected)

**OXPHOS Expression**
(Fold Change vs Con, CV-corrected)

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**MICU1 Expression**
(Fold Change vs Con, CV-corrected)

**LETM1 Expression**
(Fold Change vs Con, CV-corrected)

**VDAC Expression**
(Fold Change vs Con, CV-corrected)
SI Figure 1g, Full-length Western Blots (Figure 4d).
SI Figure 1h, Band Density Results (Figure 4d).

- NCLX Expression (Fold Change vs Con, CV-α corr.)
  - aMHC-tTA vs NCLX-Tg x tTA
  - p = 0.004

- MCU Expression (Fold Change vs Con, CV-α corr.)
  - aMHC-tTA vs NCLX-Tg x tTA

- MICU1 Expression (Fold Change vs Con, CV-α corr.)
  - aMHC-tTA vs NCLX-Tg x tTA

- VDAC Expression (Fold Change vs Con, CV-α corr.)
  - aMHC-tTA vs NCLX-Tg x tTA

- MCUb Expression (Fold Change vs Con, CV-α corr.)
  - aMHC-tTA vs NCLX-Tg x tTA

- LETM1 Expression (Fold Change vs Con, CV-α corr.)
  - aMHC-tTA vs NCLX-Tg x tTA

- EMRE Expression (Fold Change vs Con, CV-α corr.)
  - aMHC-tTA vs NCLX-Tg x tTA

- OXPHOS Expression (Fold Change vs Con)
  - CV-α, CIV-I, CII-30
  - aMHC-tTA vs NCLX-Tg x tTA