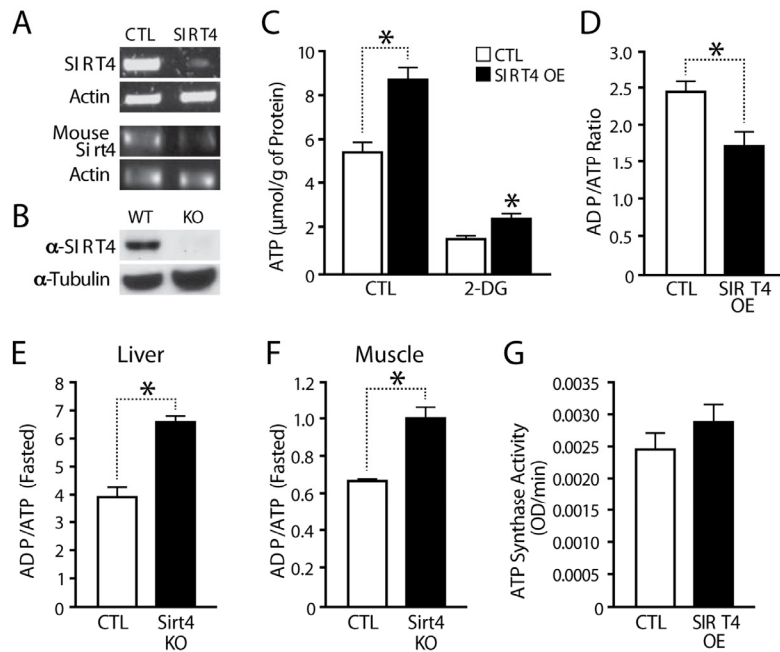
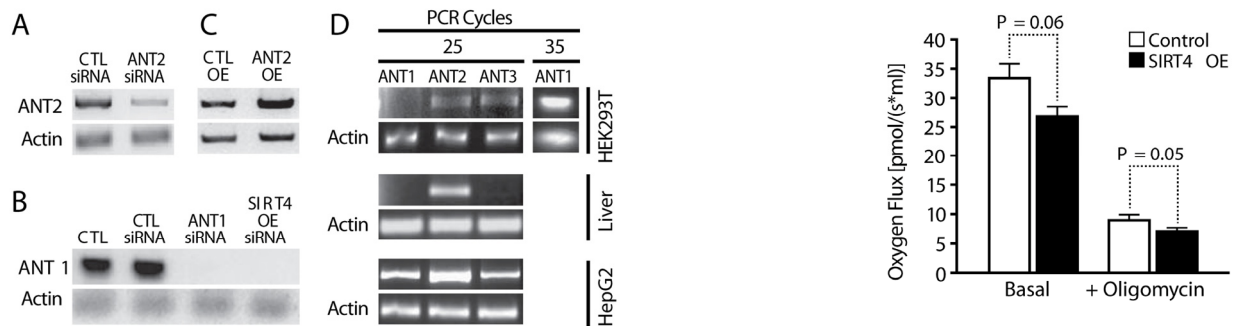


SUPPLEMENTARY INFORMATION

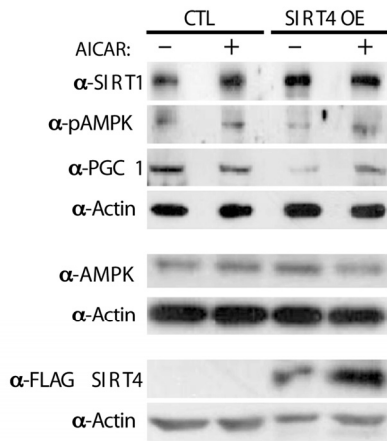


Supplementary Figure 1. (A) RT-PCR to show the efficiency of Sirt4 knockdown. (B) Western Blot using anti-Sirt4 antibodies in control and Sirt4 knockout mice. (C) Total ATP levels in control and Sirt4-overexpressing HEK293T cells, and in response to 2-deoxyglucose treatment. (D-F) ADP/ATP ratios in (D) control and Sirt4-overexpressing HEK293T cells, (E) control and Sirt4-knockout liver under fasting conditions and (F) control and Sirt4-knockout muscles under fasting conditions (G) ATP synthase activity in control and Sirt4-overexpressing HEK293T cells.

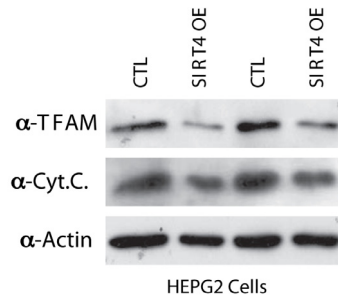


Supplementary Figure 2. (A-B) RT-PCR to show knockdown of (A) ANT2, (B) ANT1 in HEK293T cells. (C) RT-PCR to show ANT2 overexpression in HEK293T cells. (D) RT-PCR to show differential expression of ANT1, ANT2 and ANT3 in HEK293T cells, HepG2 cells and liver samples.

Supplementary Figure 3. Oxygen flux in control and Sirt4-overexpressing HEK293T cells in response to oligomycin treatment.



Supplementary Figure 4. Western blot to show the protein levels of Sirt1, phospho-AMPK, Sirt4-FLAG, PGC1 α and AMPK in control and Sirt4-overexpressing HEK293T cells, and in response to AICAR treatment.



Supplementary Figure 5. Western blot to show the protein levels of TFAM and Cytochrome-C in control and Sirt4-over-expressing HepG2 cells.

Supplementary Table 1. List of primers used for RT-qPCR

ACTIN	F: GCATGGGTCAGAAGGATTCC R: ACGCAGCTCATTGTAGAAGG
CPT1b	F: TCGTCACCTCTTCTGCCTTT R: ACACACCATAGCCGTCATCA
PGC1 α	F: GTGGATGAAGACGGATTGCC R: GCTGAGTGTGGCTGGTGCC
MCAD	F: TTGAGTTCACCGAACAGCAG R: TCCAAGTCCAAGACCTCCAC
ERR α	F: TGCCAATCAGACTCTGTGC R: CCAGCTTCACCCCATAGAAA
SIRT4	F: GACAAGGTTGATTTTGTGCAC R: TCAAAGGCAGCAACTCTCCAC
TFAM	F: CTTATAGGGCGGAGTGGCAG R: GCTGAACGAGGTCTTTTTGGT
NRF1	F: CACAGAAAAGGTGCTCAAAGGA R: TTTGGGTCCTCCGTGTTCC
CYT.C	F: GAGATGTTTCATGCGGCCAG R: ACGTAGTCCTCACCACCAT
COX-IV	F: GAGTGTTGTGAAGAGTGAA R: TCATCTCGGCGAAGCTCTC
CYT-B for mtDNA	F: CCCATCCAACATCTCCGCAT R: GATGAAAAGGCGGTTGAGGC