Table S1. Genotype distribution at weaning

Sire Genotype	Dam Genotype	Total Pups	WT	Heterozygotes	KO
$Mpc2^{+/-}$	$Mpc2^{+/-}$	78	24	54	0
$Mpc2^{\Delta 16/-}$	$Mpc2^{\Delta 16/-}$	117	29	59	29

Table S2. Embryonic Day 10-11 Genotypes

Sire Genotype	Dam Genotype	Total Pups	WT	Heterozygotes	KO
$Mpc2^{+/-}$	$Mpc2^{+/-}$	87	25	45	17

Table S3. Embryonic Day 13 Genotypes

Sire Genotype	Dam Genotype	Total Pups	WT	Heterozygotes	KO
$Mpc2^{+/-}$	$Mpc2^{+/-}$	23	9	12	2*

*Embryonic fibroblasts from KO embryos were not viable in culture.

Table S4. qPCR Primers

	Sequence (5'-3')
36B4 - FWD	GCAGACAACGTGGGCTCCAAGCAGA
36B4 - REV	GGTCCTCCTTGGTGAACACGAAGCCC
Fbp - FWD	AGCCTTCTGAGAAGGATGCTC
Fbp - REV	GTCCAGCATGAAGCAGTTGAC
G6pc - FWD	GTGGCAGTGGTCGGAGACT
G6pc - REV	ACGGGCGTTGTCCAAAC
Mpc1 - FWD	GACTTTCGCCCTCTGTTGCTA
Mpc1 - REV	GAGGTTGTACCTTGTAGGCAAAT
Mpc2 - FWD	CCGCCGCGATGGCAGCTG
Mpc2 - REV	GCTAGTCCAGCACACACCAATCC
Pcx - FWD	GATGACCTCACAGCCAAGCA
Pcx - REV	GGGTACCTCTGTGTCCAAAGGA
Pck1 - FWD	GGGTGCAGAATCTCGAGTTG
Pck1 - REV	CACCATCACCTCCTGGAAGA
Pck2 - FWD	ATGGCTGCTATGTACCTCCC
Pck2 - REV	GCGCCACAAAGTCTCGAA

Figure S1

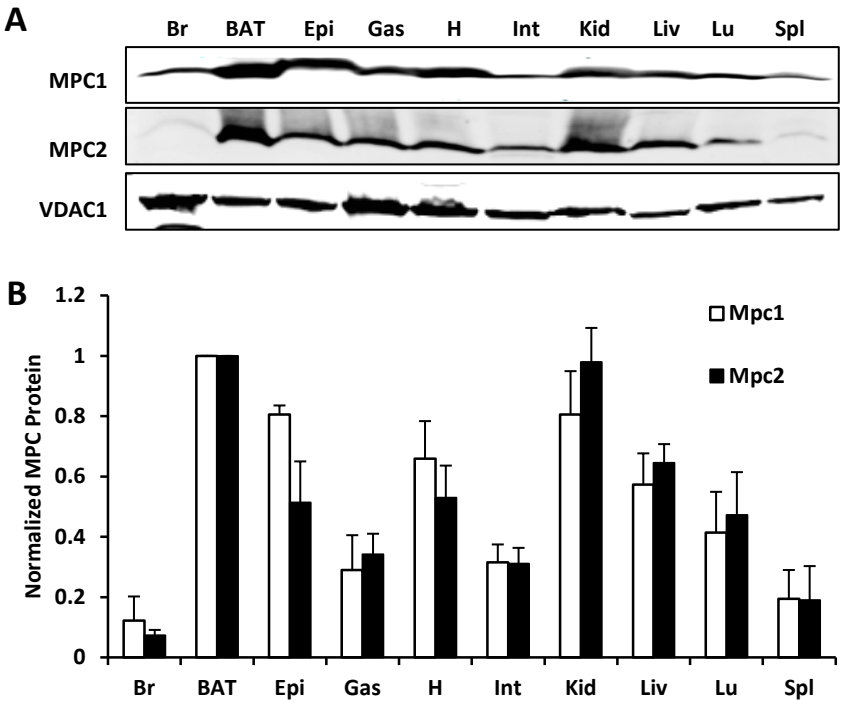

Figure S1. Tissue expression profile of MPC1 and MPC2 in WT C57B6 mice. (A) Western blot depicting the protein distribution of MPC1 and MPC2 in mitochondrial lysates of WT C57Bl/6 mice. Equal amounts of mitochondrial protein were loaded for each tissue. Voltage-dependent anion channel-1 (VDAC1) is used as a loading control. **(B)** Quantified densitometry of western blot shown in (A). Data are presented as mean ± SEM (n=3 separate animals). Abbreviations: brain (Br), brown adipose tissue (BAT), epididymal adipose tissue (Epi), perirenal adipose tissue (PR), gastrocnemius (Gas), soleus (Sol), heart (H), intestine (Int), kidney (Kid), liver (Liv), lung (Lu), and spleen (Spl). Data are presented as mean ± SEM of 5 separate animals.

Figure S2

A

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WT        – ATG GCA GCT GCC GGC GCC CGA GGC CTG CGG GCC ACC TAC CAC CGA CTC ATG
Mpc2+/-   – ATG GCA GCT GCC GGC GCC CGA GGC CTG CGG GCC ACC TAC CAC CGA CTC ATG
Mpc2Δ16   – ATG GCA GCT GCC GGC GCC CGA GGC CTG CGG GCC ACC TAC CAC CGA CTC ATG
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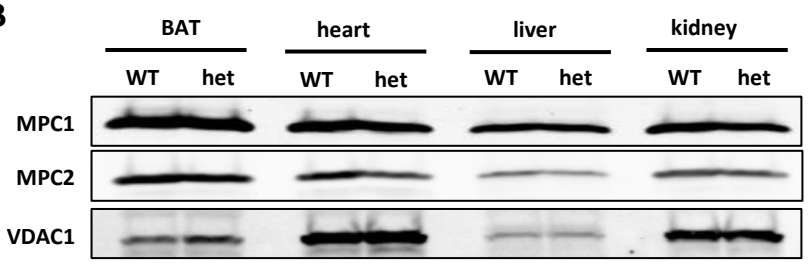
B



C

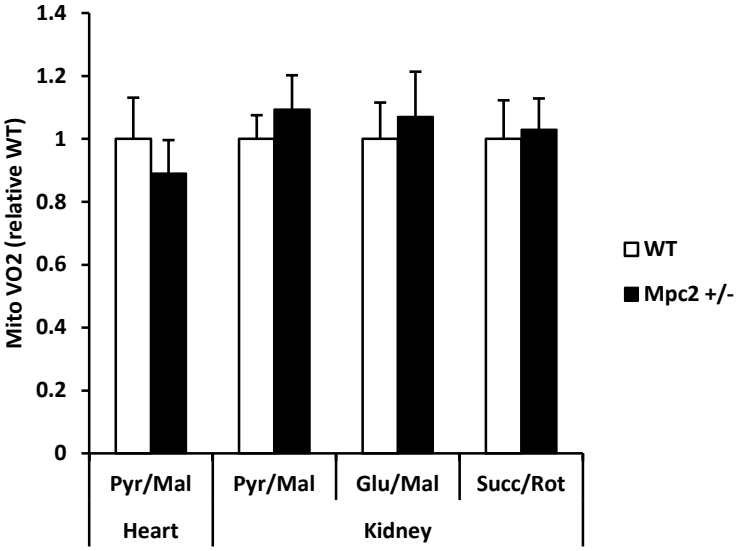


Figure S2. Generation of MPC2 deficient mice. (A) The shaded sequence indicates the deleted nucleotides for each transgenic mouse. **(B)** Western blot depicting the abundance of MPC1 and MPC2 protein in mitochondrial lysates of various tissues from $Mpc2^{+/-}$ mice and WT controls. Voltage-dependent anion channel-1 (VDAC1) is used as a loading control. **(C)** ADP-stimulated rates of oxygen consumption by mitochondria isolated from heart or kidney of WT or $Mpc2^{+/-}$ mice in the presence of the indicated substrates (n=8).

Figure S3

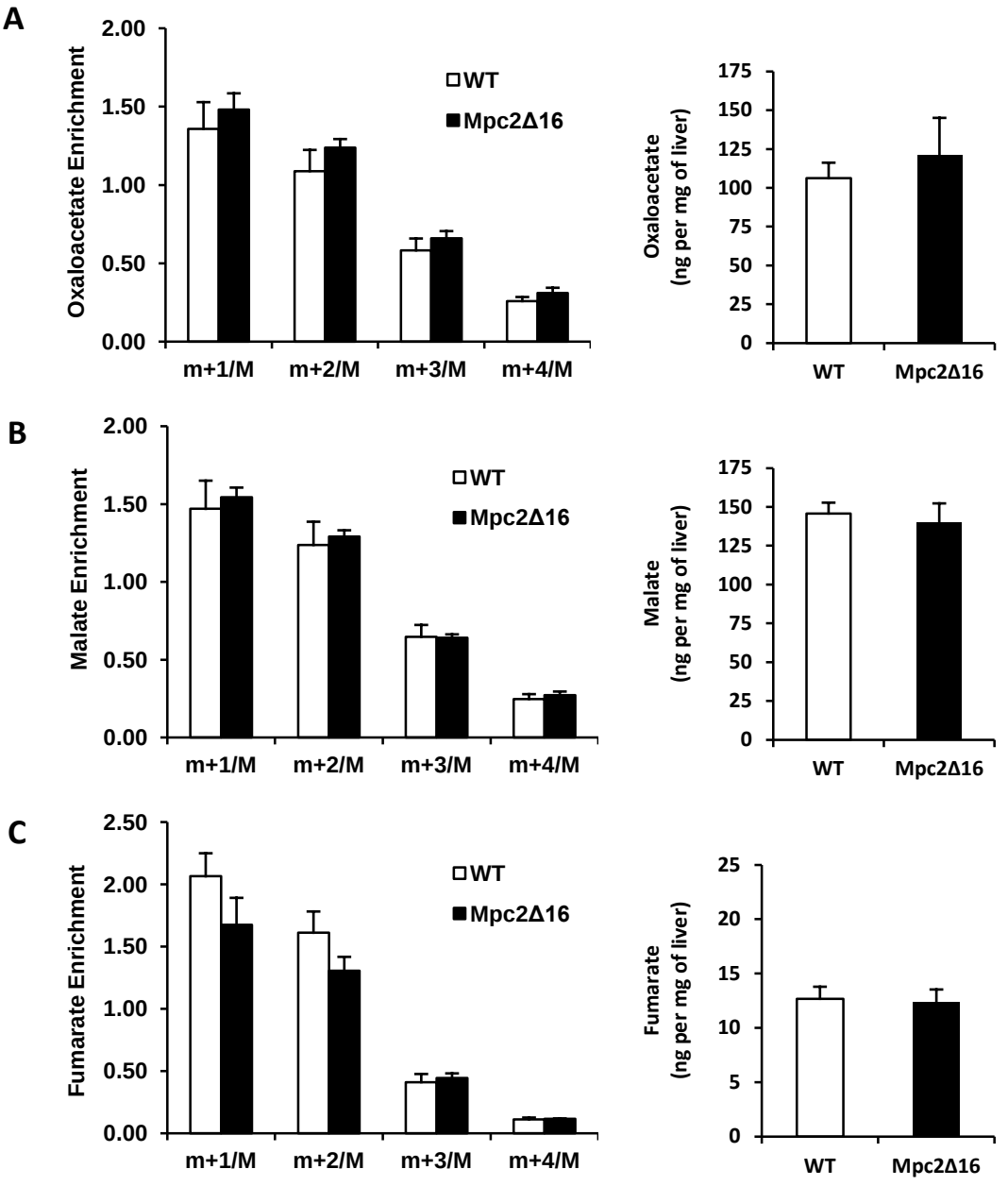


Figure S3. Hepatic organic acid enrichment and concentration are unaltered in Mpc2$^{\Delta 16}$ mice. ^{13}C enrichment of isotopomers and total concentration of hepatic oxaloacetate **(A)**, malate **(B)**, and fumarate **(C)** in mice 60 minutes after i.p. ^{13}C –pyruvate challenge (n=7). Data are presented as mean ± SEM. *P < 0.05