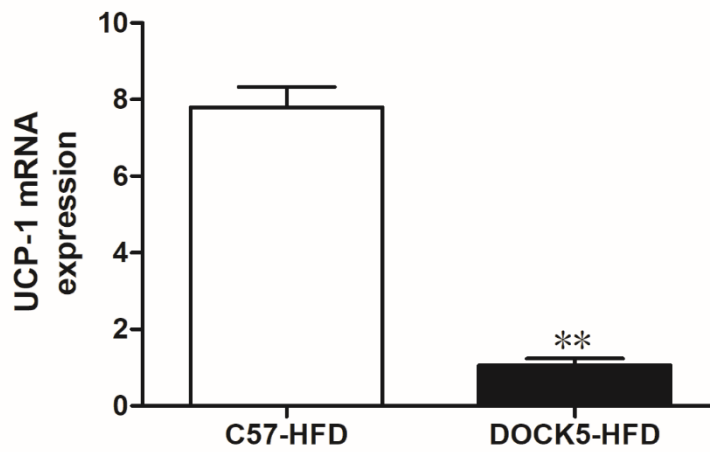


## Table Contents

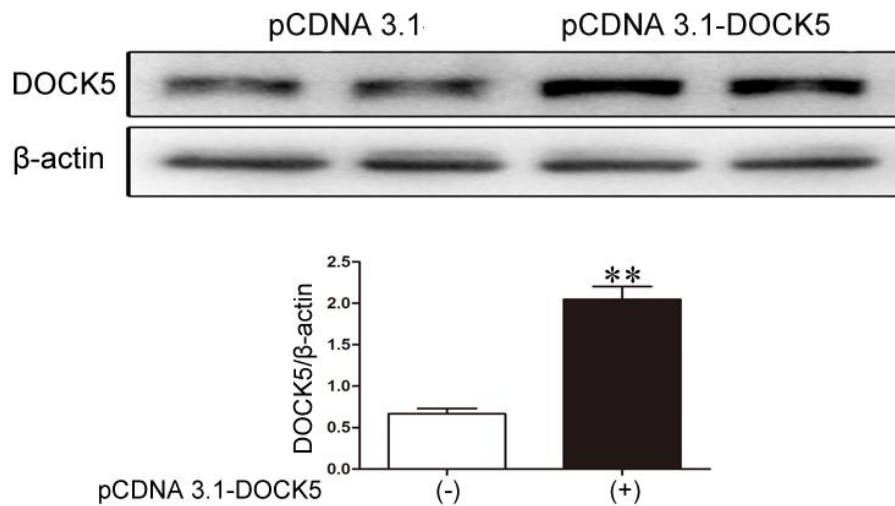
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**Appendix Figure S1 UCP1 mRNA expression in the BAT of WT and DOCK5<sup>-/-</sup> mice.**

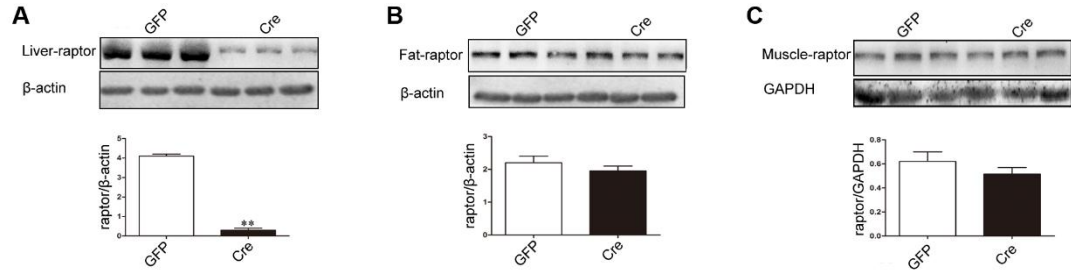
Data are expressed as the mean ± SEM. P-values were determined with *t*-test, \*\*  $p < 0.01$  vs.

WT.



**Appendix Figure S2 DOCK5 protein expression in Hep1-6 cells.**

Hep1-6 cells were infected with pCDNA3.1-DOCK5 (+) or pCDNA3.1 (-) for 48 h. Western blotting was conducted to examine DOCK5 protein expression. Data are presented as the mean  $\pm$  SEM. P-values were determined with *t*-test .\*\*  $p < 0.01$  vs. pCDNA3.1-DOCK5 (-).



**Appendix Figure S3 Raptor protein expression in AAV8-Cre- or AAV8-GFP-treated**

**Raptor<sup>flox/flox</sup> mice.**

The levels of Raptor protein expression in the

A liver

B adipose

C muscle. Data are presented as the mean  $\pm$  SEM. P-values were determined with *t*-test. \*\* *p*

< 0.01 vs. GFP group.

**Appendix Table S1** Biochemical parameters in WT and DOCK5<sup>-/-</sup> mice

Parameters	3 months				16 months			
	SD -WT	SD-DOCK5 <sup>-/-</sup>	HFD -WT	HFD -DOCK5 <sup>-/-</sup>	SD -WT	SD -DOCK5 <sup>-/-</sup>	HFD -WT	HFD-DOCK5 <sup>-/-</sup>
FBG (mmol/L)	5.20 ±0.33	5.05 ±0.49	6.80 ±0.52	7.68 ±0.28**	6.33 ±0.66	6.10 ±0.32	11.6 ±1.3	14.1 ±0.9**
FINS (mIU/L)	11.2 ±1.7	12.8 ±3.3	31.9 ±1.1	47.3 ±5.1**	18.3 ±2.5	16.5 ±3.1	77.4 ±6.30	88.5 ±3.4**
TC (mmol/L)	2.18 ±0.17	2.21 ±0.14	2.99 ±0.39	5.11 ±0.57**	2.43 ±0.24	2.39 ±0.32	6.84 ±0.73	8.20 ±0.87*
TG (mmol/L)	0.49 ±0.10	0.48 ±0.10	0.75 ±0.09	0.95 ±0.11*	0.55 ±0.07	0.53 ±0.04	1.80 ±0.31	2.46 ±0.22**
FFA (mmol/L)	0.18 ±0.03	0.22 ±0.04	0.51 ±0.14	0.82 ±0.15*	0.23 ±0.01	0.27 ±0.03	1.51 ±0.20	2.13 ±0.32*

SD, standard diet; HFD, high fat diet; FBG, fasting blood glucose; FIns, fasting plasma insulin; TC, total cholesterol; TG, triglyceride; FFA, free fatty acids.

Data are presented as means ±SD, P-values were determined with *t*-test . \**p* < 0.05, \**p* < 0.01 vs. HFD-WT.

**Appendix Table S2** Biochemical parameters in WT and DOCK5<sup>-/-</sup> mice during the HEC

Index	SD-WT (N = 6)	SD-DOCK5 <sup>-/-</sup> (N = 6)	HFD-WT (N = 6)	HFD-DOCK5 <sup>-/-</sup> (N = 6)
<b>Basal-state</b>				
BG (mmol/L)	5.43 ±0.15	5.91 ±0.19	7.02 ±0.16	7.92 ±0.31**
Ins (mIU/L)	11.0 ±1.7	11.2 ±2.0	30.9 ±2.0	48.8 ±3.1**
TC (mmol/L)	2.21 ±0.14	2.23 ±0.09	2.87 ±0.21	5.06 ±0.51**
TG (mmol/L)	0.47 ±0.07	0.49 ±0.09	0.73 ±0.06	0.97 ±0.10**
FFA ( mmol/L)	0.21 ±0.04	0.23 ±0.05	0.48 ±0.07	0.79 ±0.10**
<b>Steady-state</b>				
BG (mmol/L)	5.91 ±0.19	6.02 ±0.20	5.81 ±0.36	5.98 ±0.19
Ins (mIU/L)	80.5 ±10.7	108.6 ±19.3	240.6 ±26.9	356.3 ±32.1**
TC (mmol/L)	1.05 ±0.10	1.11 ±0.08	1.39 ±0.12	2.41 ±0.06**
TG (mmol/L)	0.16 ±0.07	0.18 ±0.04	0.37 ±0.09	0.52 ±0.08*
FFA ( mmol/L)	0.11 ±0.06	0.13 ±0.04	0.24 ±0.06	0.39 ±0.07**

FBG, fasting blood glucose; FIns, fasting plasma insulin; TC, total cholesterol; TG, triglyceride; FFA, free fatty acids; Data are presented as means ± SD, P-values were determined with *t*-test .\*\**P* < 0.01 vs. HFD-WT.

**Appendix Table S3** Biochemical parameters in HFD-fed Raptor<sup>f/f</sup> mice during the HEC

Index	GFP (n=6)	<i>shDOCK5</i> (n=6)	<i>shDOCK5</i> +Cre (n=6)
<b>Basal-state</b>			
FBG (mmol/L)	7.40 ± 0.31	8.78 ± 0.20**	7.90 ± 0.30 <sup>▲▲</sup>
FIns (mIU/L)	33.3 ± 2.51	44.3 ± 4.10**	38.2 ± 2.84 <sup>▲▲</sup>
TC (mmol/L)	2.83 ± 0.22	5.01 ± 0.31**	3.85 ± 0.42 <sup>▲▲</sup>
TG (mmol/L)	0.71 ± 0.08	0.86 ± 0.06**	0.76 ± 0.07 <sup>▲</sup>
FFA ( mmol/L)	0.56 ± 0.04	0.81 ± 0.05**	0.68 ± 0.06 <sup>▲▲</sup>
<b>Steady-state</b>			
FBG (mmol/L)	5.91 ± 0.32	5.94 ± 0.16	5.85 ± 0.17
Ins (mIU/L)	256.3 ± 27.3	348.4 ± 35.2**	297.2 ± 24.3 <sup>▲▲</sup>
TC (mmol/L)	1.23 ± 0.14	2.35 ± 0.08**	1.89 ± 0.09 <sup>▲▲</sup>
TG (mmol/L)	0.31 ± 0.07	0.48 ± 0.06**	0.40 ± 0.05 <sup>▲</sup>
FFA ( mmol/L)	0.16 ± 0.03	0.41 ± 0.05**	0.30 ± 0.06 <sup>▲▲</sup>

GFP, AAV8-GFP; *shDOCK5*, AAV8-*shDOCK5*; Cre, AAV8-Cre; FBG, fasting blood glucose; FIns, fasting plasma insulin; TC, total cholesterol; TG, triglyceride; FFA, free fatty acids; Data are presented as means ± SD, P-values were determined with one way ANOVA \*\*  $P < 0.01$  vs. GFP group; <sup>▲</sup> $P < 0.05$ , <sup>▲▲</sup> $P < 0.01$  vs. *shDOCK5* group.

**Appendix Table S4** Specific primers used for RT-PCR analyses

Gene	Forward (5'-3')	Reverse (5'-3')
DOCK5	GGGGTTGCCATCTACAACACTAC	AGCCCTCATAACATCTCCAGGA
G6Pase	GTATTGTCTCATCACCATCTTC	CGCTCACACCATCTCTTAG
PEPCK	TAGGAGCAGCCATGAGAT	CGAAGTTGTAGCCGAAGA
UCP1	CTTCCCCTGGACT	TTTCGGCAATCCTTCT
GAPDH	TGTGTCCGTCGTGGATCTGA	CCTGCTTCACCACCTTCTTGAT
$\beta$ actin	GCTGTCCCTGTATGCCTCT	GATGTCACGCACGATTTCC

DOCK5, dedicator of cytokinesis 5; G6Pase, glucose-6-phosphatase; PEPCK, phosphoenolpyruvate carboxykinase; UCP1, uncoupling protein 1; GAPDH, Glyceraldehyde 3-phosphate dehydrogenase;  $\beta$  actin, beta Actin

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