

Suppl. Table 1: Insulin injection scale

Blood sugar (mg/dl)	Insulin injection in units
200 - 349	0
350 - 400	1
401 - 460	2
461 - 510	3
511 - 600	4
≥ 600	5

Suppl. Table 2: Aperio ImageScope settings

	AGE	phospho-Smad2/3	Sirius red	TSP-1	phospho-NRF2
view width	1000	1000	1000	1000	1000
view height	1000	1000	1000	1000	1000
overlap size	0	0	0	0	0
image zoom	1	1	1	1	1
markup compression type	same as processed image	same as processed image	same as processed image	same as processed image	same as processed image
compression quality	30	30	30	30	30
classifier neighbourhood	0	0	0	0	0
classifier	none	none	none	none	none
hue value	0.1	0.1	0	0.1	0.1
hue width	0.6	0.6	0.15	0.1	0.04
color saturation threshold	0.03	0.03	0.03	0.1	0.1
lwp (high)	220	220	220	220	220
lwp (low) = lsp (high)	190	190	175	190	190
lp (low) = lsp (high)	120	120	100	120	120
lsp (low)	0	0	0	0	0
lnp (high)	-1	-1	-1	-1	-2

Lwp (high) = upper limit of total intensity of weak positive pixels, Lwp (low) = lower limit of total intensity of weak positive positive, lsp (high) = higher limit of total intensity of strong positive pixels, lsp (low) = lower limit of total intensity of strong positive pixels, lp (low) = lower limit of total intensity of positive pixels, lnp (high) = higher limit of of total intensity of negative pixels

Suppl. Table 3: Oligonucleotides for qRT-PCR evaluations

Oligonucleotides:		
Gene:	Orientation:	sequence from 5' - 3'
<i>eNOS</i>	forward	GGTCCCTCATGCCAATCTCT
	reverse	AGAACTCTTCACTCTGCCCC
<i>FAS</i>	forward	GAGGCCCATTTTGCTGTCAA
	reverse	CAGGGTGACGTTTGTTTCCA
<i>Fibronectin-1</i>	forward	TCCCGGGCAGAAAGTACATT
	reverse	TTCAGGGAGGTTGAGCTCTG
<i>Glu-Cys-ligase</i>	forward	GGGGTGACGAGGTGGAGTA
	reverse	GTTGGGGTTTGTCTCTCCC
<i>Ho-1</i>	forward	TTCAGAAGGGTCAGGTGTCC
	reverse	CAGTGAGGCCCATACCAGAA
<i>Hsf1</i>	forward	CTACGCCCAGTCAGACGTTT
	reverse	GGCTGGAGATGGAGCTGAGTA
<i>Hspa1</i>	forward	GAGATCGACTCTCTGTTGAGG
	reverse	GCCCGTTGAAGAAGTCCTG
<i>Hspa1a</i>	forward	TGGTGACAGTCCGACATGAAG
	reverse	GCTGAGAGTCGTTGAAGTAGGC
<i>Hspa1b</i>	forward	GAGATCGACTCTCTGTTGAGG
	reverse	GCCCGTTGAAGAAGTCCTG
<i>HspA8</i>	forward	TCTCGGCACCACCTACTCC
	reverse	CTACGCCCAGTCAGACGTTT
<i>iNOS</i>	forward	AATCTTGGAGCGAGTTGTGG
	reverse	CAGGAAGTAGGTGAGGGCTTG
<i>Nfe2l2</i>	forward	CGAGATATACGCAGGAGAGGTAAGA
	reverse	GCTCGACAATGTTCTCCAGCTT
<i>NfκB</i>	forward	GAAATTCCTGATCCAGACAAAAG
	reverse	ATCACTTCAATGGCCTCTGTGTAG
<i>p53</i>	forward	CCCCTGTCATCTTTGTCCCT
	reverse	AGCTGGCAGAAAGCTTATTGAG
<i>Ptgs2</i>	forward	TTCGTCGTCTCGTTGCAAAG
	reverse	CCCAGGTCCTCGCTTATGAT
<i>Renin</i>	forward	AGAACACCGTCAAACCTGGC
	reverse	CCTCTACCTTGCTTGTGGGA
<i>Sirtuin-1</i>	forward	AACATCGCAGTCTCCAAGGA
	reverse	TGCCATCATGAAGCCAGAGA
<i>Tfn-α</i>	forward	AATGGCCTCCCTCTCATCAGTT
	reverse	CCACTTGGTGGTTTGCTACGA
<i>Tgf-β</i>	forward	CAACAATTCCTGGCGTTACCTGG
	reverse	GAAAGCCCTGTATTCCGTCTCCTT
<i>Vegf</i>	forward	CGCTCCAGGATTAAACCGG
	reverse	GCTGTAACGATGAAGCCCTG
<i>VegfR</i>	forward	TGAATGTCCCACCCAGATC
	reverse	CCTCCACGTGTCTCCATTCT
<i>Wisp1</i>	forward	CAGCACCCTAGAGGAAACGA
	reverse	CTGGGCACATATCTTACAGCATT

Suppl. Table 4: Body weight

4.1 Normal diet

weeks of experiment	WT	<i>Cndp1</i> -KO	<i>p</i> (vs WT)	WT STZ	<i>p</i> (vs WT)	<i>Cndp1</i> -KO STZ	<i>p</i> (vs WT STZ)
0	19.6±1.0	19.6±1.8	0.999	19.0±1.1	0.289	19.0±1.4	0.999
12	23.2±1.3	24.6±2.3	0.339	19.8±1.8	<0.001	18.8±2.8	0.424
16	22.8±1.4	25.8±3.1	0.057	18.9±2.4	<0.001	19.7±2.6	0.674
20	24.1±1.7	27.1±3.5	0.115	19.3±2.2	<0.001	19.8±2.8	0.868
24	24.2±1.9	27.0±3.3	0.134	19.6±2.3	<0.001	19.7±2.8	0.999
28	24.7±1.2	27.9±3.9	0.110	19.6±2.5	<0.001	20.3±2.6	0.819
30	24.3±1.8	28.5±4.1	0.044	19.9±2.3	0.001	20.2±2.7	0.989
32	23.9±1.6	27.8±4.4	0.086	19.5±2.1	<0.001	19.9±3.1	0.950
average	23.3±1.5	26.0±2.7	0.017	19.4±0.3	0.001	19.6±0.5	0.993

4.2 High fat diet

weeks of experiment	WT HFD	<i>Cndp1</i> -KO HFD	<i>p</i> (vs WT HFD)	<i>p</i> (vs WT ND)	<i>p</i> (vs <i>Cndp1</i> -KO ND)	WT HFD + STZ	<i>p</i> (vs WT HFD)	<i>Cndp1</i> -KO HFD + STZ	<i>p</i> (vs WT HFD STZ)
0	19.8±1.7	19.1±1.5	0.667	0.986	0.9915	18.7±1.4	0.240	19.8±2.0	0.118
12	32.6±5.0	35.2±6.1	0.616	0.116	<0.001	19.4±1.9	<0.001	21.2±1.8	0.010
16	36.1±5.3	39.8±6.2	0.357	0.010	<0.001	20.8±2.0	<0.001	22.0±2.7	0.304
20	39.5±4.6	42.5±6.4	0.465	0.002	<0.001	20.7±1.7	<0.001	21.9±2.7	0.280
24	41.6±4.8	45.5±7.5	0.320	0.001	<0.001	20.9±1.7	<0.001	22.3±1.9	0.055
28	45.5±5.3	49.2±7.4	0.406	<0.001	<0.001	21.3±1.7	<0.001	22.4±2.6	0.479
30	43.5±5.4	49.5±7.4	0.082	<0.001	<0.001	21.5±1.9	<0.001	23.4±2.3	0.059
32	42.8±4.8	48.6±7.9	0.083	<0.001	<0.001	21.7±2.7	<0.001	23.0±2.2	0.337
average	37.7±7.1	41.1±9.6	0.723	<0.001	<0.001	20.6±0.9	0.001	22.0±1.0	0.975

Statistical analyses were performed with mixed effect models. n=10-29 per group. Data are mean ± SD gram body weight.

Suppl. Table 5: Energy intake

5.1 Normal diet

weeks of experiment	WT	<i>Cndp1</i> -KO	<i>p</i> (vs WT)	WT STZ	<i>p</i> (vs WT)	<i>Cndp1</i> -KO STZ	<i>p</i> (vs WT STZ)
12	36.4±3.1	41.1±8.7	0.616	53.6±15.9	0.008	53.6±16.4	1.000
16	37.4±3.8	35.9±8.1	0.975	54.9±9.6	0.001	54.1±13.3	0.998
20	33.5±6.1	39.6±5.6	0.364	50.7±8.8	0.004	58.5±15.3	0.351
24	35.7±3.4	45.2±5.7	0.035	46.8±11.0	0.039	57.5±8.9	0.080
28	37.2±5.9	43.0±7.2	0.492	49.4±11.4	0.072	52.1±9.7	0.933
Average	36.0±4.4	40.9±7.0	0.323	51.0±11.3	<0.001	55.1±12.7	0.133

5.2 High fat diet

weeks of experiment	WT HFD	<i>Cndp1</i> -KO HFD	<i>p</i> (vs WT HFD)	WT HFD STZ	<i>p</i> (vs WT HFD)	<i>Cndp1</i> -KO HFD STZ	<i>p</i> (vs WT HFD STZ)
12	30.9±5.4	40.7±9.6	0.17	60.2±12.9	0.001	60.7±17.2	0.999
16	56.8±6.4	48.6±9.4	0.341	52.7±7.6	0.712	54.2±8.5	0.998
20	33.7±12.2	47±16.9	0.451	56.5±10.3	0.078	62.7±12.7	0.351
24	37.2±6.8	40.2±7.4	0.890	54.7±7.6	0.020	59.1±14.0	0.080
28	37.1±14.0	49.4±9.3	0.468	57.1±9.2	0.172	65.1±8.2	0.933
average	39.6±7.6	44.1±10.8	0.543	56.0±9.6	<0.001	59.1±13.0	0.501

Statistical analyses were performed with mixed effect model, n=6-16 per group. Data are mean ± SD in kJ/mouse/24h.

Suppl. Table 6: Liquid intake

6.1 Normal diet

weeks of experiment	WT	<i>Cndp1</i> -KO	<i>p</i> (vs WT)	WT STZ	<i>p</i> (vs WT)	<i>Cndp1</i> -KO STZ	<i>p</i> (vs WT STZ)
12	4.2±0.2	4.9±1.2	0.492	17.8±4.5	<0.001	18.6±6.7	0.976
16	4.3±0.5	4.5±0.8	0.936	19.2±4.0	<0.001	19.0±5.7	0.999
20	4.1±0.5	4.6±0.7	0.354	17.4±4.3	<0.001	21.3±6.3	0.249
24	4.5±0.3	4.9±0.7	0.429	14.8±3.7	<0.001	17.7±3.7	0.294
28	4.3±0.2	4.5±0.8	0.921	16.5±4.9	0.001	19.1±5.2	0.653
average	4.2±0.3	4.6±0.8	0.983	17.1±4.2	<0.001	19.1±5.5	0.041

6.2 High fat diet

weeks of experiment	WT HFD	<i>Cndp1</i> -KO HFD	<i>p</i> (vs WT HFD)	WT HFD STZ	<i>p</i> (vs WT HFD)	<i>Cndp1</i> -KO HFD STZ	<i>p</i> (vs WT HFD STZ)
12	2.8±0.6	3.4±0.8	0.476	12.3±2.7	<0.001	12.3±4.1	0.999
16	3.1±0.4	3.2±0.6	0.955	11.9±3.1	<0.001	9.6±3.3	0.281
20	2.4±1.0	3.0±0.8	0.713	12.1±3.7	<0.001	12.3±2.0	0.998
24	2.4±0.5	2.9±0.6	0.364	12.3±3.5	<0.001	12.6±2.3	0.992
28	2.4±0.5	3.1±0.7	0.190	11.8±5.2	0.001	13.1±3.4	0.895
average	2.6±0.5	3.1±0.7	0.904	12.0±3.6	<0.001	12.0±3.0	0.998

Statistical analyses were performed with mixed effect models. n=6-17 per group. Data are mean ± SD g water/mouse/24h.

Suppl. Table 7: Fasting blood glucose levels

7.1 Normal diet

weeks of experiment	WT	<i>Cndp1</i> -KO	<i>p</i> (vs WT)	WT STZ	<i>p</i> (vs WT)	<i>Cndp1</i> -KO STZ	<i>p</i> (vs WT STZ)
12	6.5±1	7.5±1.3	0.205	21.5±5	<0.001	20.2±5	0.792
16	6.3±0.5	7.4±1.2	0.073	21.6±4.8	<0.001	21.2±4.5	0.991
20	6.6±1.1	7.5±1.4	0.369	20.4±4.5	<0.001	22.9±4.5	0.206
24	7.2±1.0	6.6±2.2	0.878	21.3±5.9	<0.001	21.3±3.0	1.000
28	6.5±0.8	7.0±1.5	0.772	20.4±4.8	<0.001	19.6±4.2	0.935
30	7.5±1.4	6.9±0.9	0.599	19.4±4.9	<0.001	19.2±6.5	1.000
32	6.5±0.8	7.3±0.8	0.132	19.3±4.5	<0.001	20.6±3.1	0.751
average	6.7±0.4	7.1±0.4	0.745	20.5±1.0	<0.001	20.7±1.2	0.982

7.2 High fat diet

weeks of experiment	WT HFD	<i>Cndp1</i> -KO HFD	<i>p</i> (vs WT HFD)	WT HFD STZ	<i>p</i> (vs WT HFD)	<i>Cndp1</i> -KO HFD STZ	<i>p</i> (vs WT HFD STZ)
12	8.0±1.5	7.7±0.9	0.879	20.1±2.7	<0.001	19.8±3.0	0.994
16	7.9±1.0	8.4±1.5	0.672	21.5±3.1	<0.001	20.0±3.1	0.356
20	8.2±1.0	9.4±1.6	0.064	21.3±2.8	<0.001	20.7±2.6	0.899
24	9.5±1.4	8.6±1.8	0.451	21.9±3.9	<0.001	20.7±3.4	0.729
28	8.8±1.5	8.1±1.4	0.684	22.7±4.3	<0.001	21.0±3.6	0.568
30	8.3±1.2	8.4±1.0	0.987	21.4±4.1	<0.001	21.6±4.6	0.999
32	8.7±1.2	8.8±1.1	0.972	20.8±4.0	<0.001	20.2±3.6	0.961
average	8.4±0.5	8.5±0.6	0.999	21.3±0.8	<0.001	20.6±0.6	0.125

Statistical analyses were performed with mixed effect model. n=10-27 per group. Data are mean ± SD in Blood glucose levels in mmol/l.

Suppl. Table 8: Kidney protein expression of HSP70 protein family members, carnosine synthase 1, phospho-NRF2 and thrombospondin-1

8.1 Normal diet							
Protein	WT	<i>Cndp1</i> -KO	<i>p</i> (vs WT)	WT STZ	<i>p</i> (vs WT)	<i>Cndp1</i> -KO STZ	<i>p</i> (vs WT STZ)
HSPA1A/A1B	1.0±0.6	0.9±0.6	0.999	1.1±0.6	0.999	1.9±2.0	0.774
HSPA9	1.0±0.3	1.0±0.4	1.000	1.3±0.4	0.815	1.2±0.2	0.994
HSP60	1.0±1.1	1.6±1.4	0.841	0.7±0.4	0.970	0.7±0.3	0.999
HSF1	1.0±0.4	1.1±0.1	1.000	2.0±1.6	0.493	1.6±0.5	0.966
Carnosine Synthase 1	0.6±0.2	0.4±0.3	0.443	0.3±0.2	0.107	0.3±0.3	1.000
Phospho-NRF2	0.4±0.1	0.3±0.2	0.403	0.3±0.1	0.911	0.3±0.1	0.403
Thrombospondin-1	1.0±0.6	1.1±1.1	0.994	0.9±0.6	0.981	1.2±0.9	0.818

8.2. High fat diet							
Protein	WT HFD	<i>Cndp1</i> -KO HFD	<i>p</i> (vs WT HFD)	WT HFD STZ	<i>p</i> (vs WT HFD)	<i>Cndp1</i> -KO HFD STZ	<i>p</i> (vs WT HFD STZ)
Carnosine synthase 1	0.5±0.2	0.4±0.1	0.568	0.3±0.3	0.130	0.6±0.3	0.021
Phospho-NRF2	0.3±0.1	0.2±0.1	0.828	0.3±0.1	0.969	0.3±0.2	0.908
Thrombospondin-1	1.1±0.6	0.9±0.6	0.752	1.2±0.7	0.999	1.2±0.6	0.999

Statistical analyses were performed with one-way ANOVA. n=4 per group. Data are mean ± SD. For HSP-70 proteins, data were normalized to WT.