

ESM Table 1. Transcript abundance of Nrf2 target genes in Control and STZ- diabetic mice

	A (WT-EE)	B (WT-LE)	C (WT-LH)	D (STZ-HH)	E (STZ-LE)	F (STZ-LH)
<i>Nrf2</i>	1.0±0.04	0.98±0.05	1.16±0.12	1.48±0.03*	1.28±0.08*	1.79±0.12*
<i>Nqo1</i>	1.0±0.03	0.94±0.03	0.87±0.03	1.53±0.15*	1.39±0.19	1.53±0.09*
<i>Sod2</i>	0.99±0.04	4.83±0.03*	0.59±0.51	5.73±0.61*	0.69±0.06	1.67±0.11*
<i>Hmox-1</i>	0.99±0.09	1.42±0.10*	0.92±0.10	0.85±0.05	0.89±0.04	1.11±0.11

Control (WT) mice, groups A-C; Type 1 diabetic (STZ) mice, groups D-F. Clamp protocols: E = Euglycemia, L = Hypoglycaemia, H = Hyperglycaemia. Ratios presented relative (to A (EEE)) gene expression of NAD(P)H: quinoneoxidoreductase 1 (*Nqo1*), superoxide dismutase 2 (*Sod2*), hemeoxygenase 1 (*Hmox-1*), $n = 10-12$ /group. Data were analysed by Kruskal-Wallis with Dunn's multiple comparisons test. Results represent mean values \pm SEM. * $P < 0.05$, vs WT-EE

ESM Table 2. Transcript abundance of Nrf2 target genes in *Nrf2*^{-/-} mice

	G (Nrf-EE)	H (Nrf2-LE)	I (Nrf2-LH)
<i>Nqo1</i>	1.0±0.04	0.99±0.09	0.94±0.03
<i>Sod2</i>	0.99±0.14	1.14±0.21	0.91±0.10
<i>Hmox-1</i>	0.99±0.18	1.18±0.32	0.97±0.10

Nrf2^{-/-} mice, groups G-I. $n = 8-10$ /group. Data were analysed by Kruskal-Wallis with Dunn's multiple comparisons test. Results represent mean values \pm SEM

ESM Table 3. Upregulated proteins

Protein names	Gene names	Fold change	p value
Coiled-coil domain-containing protein 47	<i>Ccdc47</i>	1.28	0.0066
Non-specific lipid-transfer protein	<i>Scp2</i>	1.26	0.0279
Serine/threonine-protein phosphatase 4 regulatory subunit 2	<i>Ppp4r2</i>	1.24	0.0134
Alanine--tRNA ligase, cytoplasmic	<i>Aars</i>	1.18	0.0050
Thyroid hormone receptor-associated protein 3	<i>Thrap3</i>	1.18	0.0075
SWI/SNF complex subunit SMARCC2	<i>Smarcc2</i>	1.18	0.0434
Trifunctional enzyme subunit alpha, mitochondrial;Long-chain enoyl-CoA hydratase;Long chain 3-hydroxyacyl-CoA dehydrogenase	<i>Hadha</i>	1.14	0.0233
Phosphatidylinositol 5-phosphate 4-kinase type-2 gamma	<i>Pip4k2c</i>	1.13	0.0100
Trifunctional enzyme subunit beta, mitochondrial;3-ketoacyl-CoA thiolase	<i>Hadhb</i>	1.13	0.0242
Proteasome subunit alpha type-2	<i>Psm2</i>	1.13	0.0439
Small acidic protein	<i>Smad1;1110004F10Rik</i>	1.12	0.0396
6-phosphogluconate dehydrogenase, decarboxylating	<i>6Pgd</i>	1.11	0.0195
Long-chain specific acyl-CoA dehydrogenase, mitochondrial	<i>Acadl</i>	1.11	0.0369
Lupus La protein homolog	<i>Ssb</i>	1.10	0.0244
Isoleucine--tRNA ligase, mitochondrial	<i>Iars2</i>	1.09	0.0130
D-beta-hydroxybutyrate dehydrogenase, mitochondrial	<i>Bdh1</i>	1.09	0.0446
Ornithine aminotransferase, mitochondrial	<i>Oat</i>	1.09	0.0426
Heterochromatin protein 1-binding protein 3	<i>Hp1bp3</i>	1.09	0.0222
Carbonyl reductase [NADPH] 1	<i>Cbr1</i>	1.09	0.0023
Plastin-3	<i>Pls3</i>	1.09	0.0312
Proteasome subunit alpha type-3	<i>Psm3</i>	1.09	0.0186
Neurochondrin	<i>Ncdn</i>	1.09	0.0342
Fructose-bisphosphate aldolase C	<i>Aldoc</i>	1.08	0.0289
Lamin-B1	<i>Lmnb1</i>	1.08	0.0180
60S acidic ribosomal protein P1	<i>Rplp1;Gm10073</i>	1.08	0.0384
Succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial;Succinyl-CoA:3-ketoacid-coenzyme A transferase	<i>Oxct1</i>	1.07	0.0196
Proteasome subunit beta type-7	<i>Psm7</i>	1.07	0.0403
Electron transfer flavoprotein subunit alpha, mitochondrial	<i>Etfa</i>	1.06	0.0343
Nucleolin	<i>Ncl</i>	1.06	0.0493
NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 3	<i>Ndufb3</i>	1.06	0.0388
Protein DJ-1	<i>Park7</i>	1.05	0.0162
Ubiquitin carboxyl-terminal hydrolase;Ubiquitin carboxyl-terminal hydrolase 14	<i>Usp14</i>	1.05	0.0228
Acyl carrier protein;Acyl carrier protein, mitochondrial	<i>Ndufab1</i>	1.05	0.0185
NADH dehydrogenase [ubiquinone] iron-sulfur protein 6, mitochondrial	<i>Ndufs6</i>	1.05	0.0401
Aldehyde dehydrogenase, mitochondrial	<i>Aldh2</i>	1.05	0.0137
Phosphoglucomutase-1	<i>Pgm1;Pgm2</i>	1.05	0.0285
Actin-binding LIM protein 1	<i>Ablim1</i>	1.04	0.0459
Guanine nucleotide-binding protein G(i) subunit alpha-1	<i>Gnai1</i>	1.03	0.0014

ESM Table 4. Downregulated proteins

Protein names	Gene names	Fold change	p value
Ubiquitin carboxyl-terminal hydrolase;Ubiquitin carboxyl-terminal hydrolase 5	<i>Usp5</i>	0.96	0.0164
Myosin-10	<i>Myh10</i>	0.96	0.0469
Microtubule-associated protein tau	<i>Mapt</i>	0.96	0.0397
AP2-associated protein kinase 1	<i>Aak1</i>	0.95	0.0331
Heat shock cognate 71 kDa protein	<i>Hspa8</i>	0.95	0.0234
Epidermal growth factor receptor substrate 15-like 1	<i>Eps15l1</i>	0.95	0.0390
Thy-1 membrane glycoprotein	<i>Thy1</i>	0.95	0.0401
Calcineurin subunit B type 1	<i>Ppp3r1</i>	0.95	0.0228
Cytosolic acyl coenzyme A thioester hydrolase	<i>Acot7</i>	0.95	0.0341
Kinesin-like protein KIF2A	<i>Kif2a</i>	0.94	0.0219
AP-3 complex subunit delta-1	<i>Ap3d1</i>	0.94	0.0189
Synaptosomal-associated protein 25	<i>Snap25</i>	0.93	0.0166
Glutaredoxin-3	<i>Glrx3</i>	0.93	0.0139
Serine/threonine-protein kinase PAK 1	<i>Pak1</i>	0.93	0.0100
Elongation factor Tu, mitochondrial	<i>Tufm</i>	0.93	0.0016
Cysteine and histidine-rich domain-containing protein 1	<i>Chordc1</i>	0.92	0.0410
Gamma-aminobutyric acid receptor-associated protein-like 2	<i>Gabarapl2</i>	0.91	0.0118
Cofilin-2	<i>Cfl2</i>	0.91	0.0428
Coronin;Coronin-1A	<i>Coro1a</i>	0.91	0.0407
Stress-induced-phosphoprotein 1	<i>Stip1</i>	0.90	0.0003
Rho-associated protein kinase 2	<i>Rock2</i>	0.90	0.0451
AMP deaminase 2	<i>Ampd2</i>	0.90	0.0109
Mitochondrial glutamate carrier 1	<i>Slc25a22</i>	0.90	0.0176
Calcyclin-binding protein	<i>Cacybp</i>	0.89	0.0300
Glycogen debranching enzyme	<i>Agl</i>	0.88	0.0397
Alpha-adducin	<i>Add1</i>	0.88	0.0323
Hsp90 co-chaperone Cdc37	<i>Cdc37</i>	0.88	0.0101
Heat shock protein HSP 90-alpha	<i>Hsp90aa1</i>	0.88	0.0119
Peptidyl-prolyl cis-trans isomerase D	<i>Ppid</i>	0.88	0.0089
Heat shock protein HSP 90-beta	<i>Hsp90ab1</i>	0.87	0.0261
Glucose 1,6-bisphosphate synthase	<i>Pgm2L1</i>	0.87	0.0226
Protein lunapark	<i>Lnp</i>	0.86	0.0127
ETS translocation variant 2	<i>Etv2</i>	0.86	0.0439
Clusterin;Clusterin beta chain;Clusterin alpha chain	<i>Clu</i>	0.86	0.0078
cGMP-dependent 3,5-cyclic phosphodiesterase	<i>Pde2a</i>	0.85	0.0394
Nuclear migration protein nudC	<i>Nudc</i>	0.85	0.0221
Small glutamine-rich tetratricopeptide repeat-containing protein beta	<i>Sgtb</i>	0.83	0.0130
Heat shock protein 105 kDa	<i>Hsph1</i>	0.83	0.0028
CD99 antigen-like protein 2	<i>Cd99l2</i>	0.78	0.0324
Hydroxymethylglutaryl-CoA synthase, cytoplasmic	<i>Hmgcs1</i>	0.78	0.0388
5-nucleotidase domain-containing protein 3	<i>Nt5dc3</i>	0.72	0.0267