Supplementary data

Suppl. Fig. 1 Blood glucose and plasma parameters

A Blood glucose levels of TallyHo mice at 9 weeks of age. **B-C** Plasma glycerol and C-reactive protein levels (CRP) at 17 weeks of age. **D** Plasma glucose levels of BEZ treated TallyHo mice at 17 weeks of age. **E-F** Plasma insulin levels during glucose tolerance test at 16 weeks of age. Columns represent averages ± standard deviations; n=7-12. * denotes significant differences between ED, BEZ vs. ED, SD; *p<0.05, ***p<0.001; **#** denotes significant differences between ED, SD vs. LD, SD; ##p<0.01, ###p<0.001; **§** denotes significant differences between LD, BEZ vs. LD, SD; §§§p<0.001.

Suppl. Fig. 2 Pancreas architecture

Pancreata were stained with anti-insulin and anti-glucagon antibodies and visualized by fluorescence microscopy. Glucagon area was normalized to **A** islet area or **B** total pancreas area. Columns represent averages ± standard deviations; n=5. # denotes significant differences between ED, SD vs. LD, SD; #p<0.05.

Suppl. Fig. 3 Body composition and food/water intake

A Fat and **B** lean mass were measured by qNMR and **C-D** adjusted to body weights, p-values are indicated. **E** Food consumption and **F** water intake were determined using indirect calorimetry. Columns represent averages ± standard deviations; n=8-9. **#** denotes significant differences between ED, SD vs. LD, SD; #p<0.05, ##p<0.01, ###p<0.001; **§** denotes significant differences between LD, BEZ vs. LD, SD; §p<0.05, §§p<0.01, §§§p<0.001.

Suppl. Fig. 4 Indirect calorimetry

A Oxygen consumption (VO_2), **C** carbon dioxide production (VCO_2), **E** run distance and **G** rearing were measured and appropriate mean values were calculated **B, D, F, H**. Gray rectangle represents 12 h dark phase (0 time point represents 1 p.m.). Columns represent averages ± standard deviations; n=8-9. * denotes significant differences between ED, BEZ vs. ED, SD; *p<0.05, ***p<0.001.

Suppl. Fig. 5 Euglycemic-hyperinsulinemic clamp and hepatic triglyceride content

A Glucose uptake rate in quadriceps muscle and epididimal white adipose tissue (epWAT). **B** Urine glucose measurement**. C-D** PUFA n-6 or n-3 fatty acids in hepatic TG fraction. Columns represent averages ± standard deviations; n=5-11. * denotes significant differences between ED, BEZ vs. ED, SD; *p<0.05, **p<0.01, ***p<0.001; § denotes significant differences between LD, BEZ vs. LD, SD; §p<0.05.

Suppl. Fig. 6 Hepatic citrate synthase protein level and mitochondrial gene expression

A Hepatic citrate synthase (CS) protein level was analyzed using Western blot and representative samples are depicted. The intensity of the bands were normalized to tubulin as loading control by densitometry and shown as Fig. 6C. **B-E** Hepatic mitochondrial gene expression was studied using real-time PCR and results were normalized to *Rps2* as housekeeping gene and depicted as ratio to LD, SD group. *Ndufab1*: NADH dehydrogenase (ubiquinone) 1, alpha/beta subcomplex, 1, *Cox19*: cytochrome c oxidase assembly protein 19, *Cpt2*: carnitine palmitoyltransferase 2, *Hadha*: hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl-Coenzyme A thiolase/enoyl-Coenzyme A hydratase (trifunctional protein), alpha subunit. Columns represent averages ± standard deviations; n=4-8. * denotes significant differences between ED, BEZ vs. ED, SD; *p<0.05, **p<0.01, ***p<0.001; § denotes significant differences between LD, BEZ vs. LD, SD; §§p<0.01, §§§p<0.001.

Suppl. Fig. 7 Mitochondrial mass in skeletal muscle

Mitochondrial mass was studied in **A** red and **B** white muscle of quadriceps at 10.000x and 20.000x magnification, respectively. Black bars denote **A** 500 nm and **B** 200 nm, respectively. Representative areas are shown, n=4.

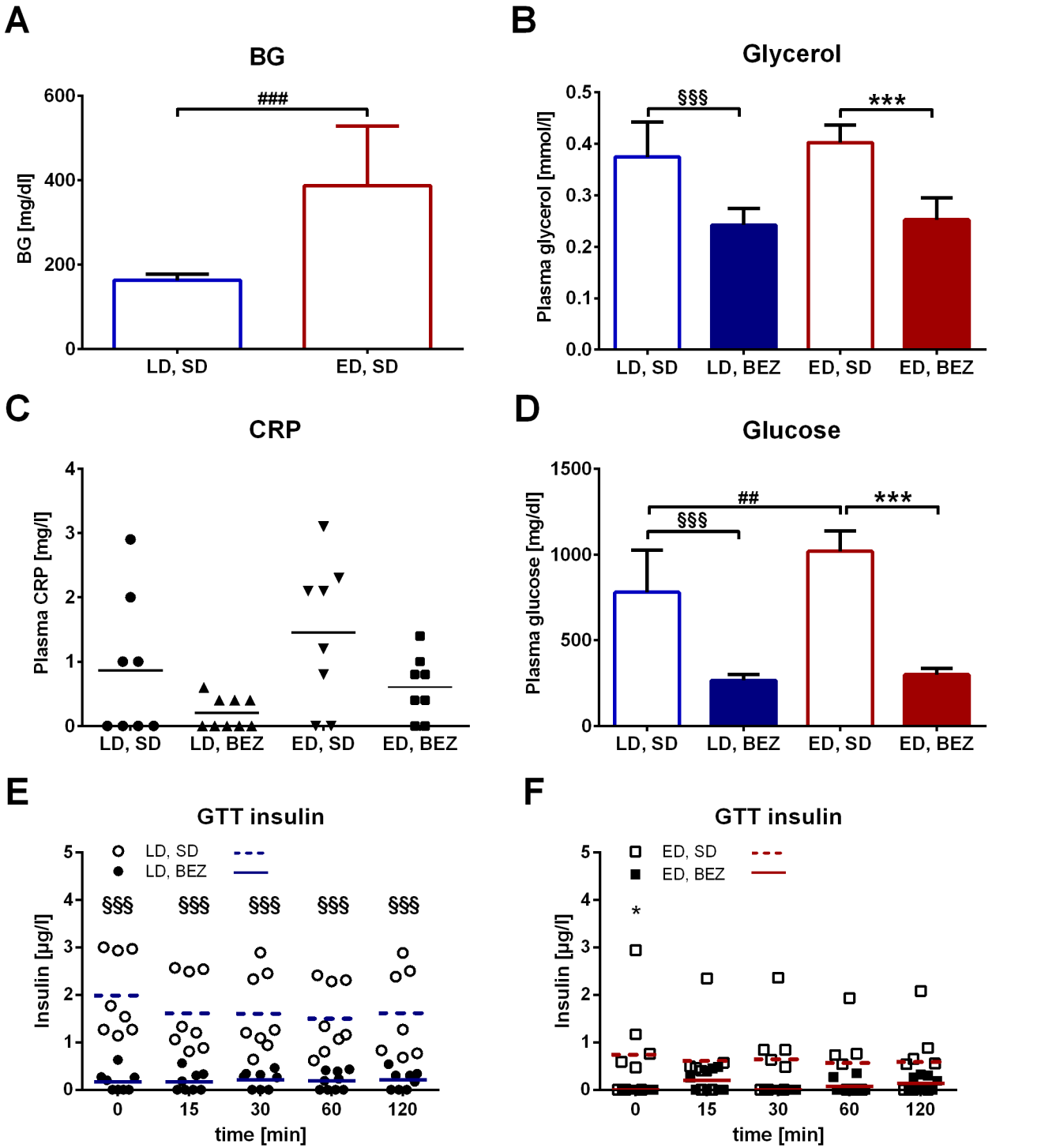
Supplementary Table 1 Absolute FA composition of hepatic TG fraction

		av±st dev	av±st dev	av±st dev	av±st dev	Holm-Sídáks´test	Holm-Sídáks´test	Holm-Sídáks´test
n	**FA**	**LD, SD**	**LD, BEZ**	**ED, SD**	**ED, BEZ**	**ED, SD vs LD, SD**	**LD, BEZ vs LD, SD**	**ED, BEZ vs ED, SD**
	C14:0	1.668±0.652	0.316±0.086	0.182±0.062	0.307±0.052	p<0.001	p<0.001	ns
	C16:0	60.59±21.72	12.27±3.101	8.744±3.208	11.38±1.498	p<0.001	p<0.001	ns
	C18:0	4.110±0.788	1.113±0.397	1.947±0.625	0.964±0.265	p<0.001	p<0.001	p<0.05
	C20:0	0.603±0.103	0.034±0.010	0.074±0.046	0.032±0.013	p<0.001	p<0.001	ns
	C22:0	0.104±0.032	0.036±0.018	0.229±0.411	0.034±0.017	ns	ns	ns
	C24:0	0.014±0.005	0.011±0.005	0.012±0.007	0.010±0.003	ns	ns	ns
	C26:0	0.012±0.007	0.019±0.010	0.013±0.005	0.018±0.004	ns	ns	ns
n7	**cC16:1**	8.514±4.079	1.176±0.406	0.164±0.130	1.003±0.263	p<0.001	p<0.001	ns
n10	**C16:1**	3.181±1.114	0.637±0.186	0.254±0.120	0.641±0.118	p<0.001	p<0.001	ns
n7	**cC18:1**	9.279±3.884	1.251±0.437	0.304±0.195	1.096±0.283	p<0.001	p<0.001	ns
n9	**C18:1**	63.80±27.40	6.003±1.885	3.102±1.772	5.271±1.469	p<0.001	p<0.001	ns
n9	**C24:1**	0.005±0.001	0.034±0.051	0.007±0.001	0.009±0.001	ns	ns	ns
n6	**C18:2**	22.80±2.987	2.887±0.347	4.869±0.918	2.523±0.610	p<0.001	p<0.001	p<0.05
n6	**C18:3**	0.386±0.066	0.091±0.020	0.123±0.029	0.082±0.008	p<0.001	p<0.001	ns
n6	**C20:3**	0.797±0.234	0.227±0.033	0.219±0.059	0.199±0.036	p<0.001	p<0.001	ns
n6	**C20:4**	0.910±0.293	0.189±0.011	0.338±0.050	0.153±0.041	p<0.001	p<0.001	ns
n6	**C22:4**	0.227±0.108	0.045±0.008	0.098±0.017	0.038±0.008	p<0.01	p<0.001	ns
n6	**C22:5**	0.090±0.042	0.028±0.013	0.043±0.012	0.019±0.004	p<0.05	p<0.01	ns
n6	**C24:4**	0.008±0.007	0.010±0.004	0.012±0.008	0.007±0.003	ns	ns	ns
n6	**C24:5**	0.011±0.004	0.014±0.008	0.013±0.004	0.013±0.004	ns	ns	ns
n3	**C18:3**	1.015±0.207	0.073±0.005	0.119±0.027	0.061±0.012	p<0.001	p<0.001	ns
n3	**C18:4**	0.030±0.009	0.011±0.003	0.012±0.005	0.013±0.002	p<0.001	p<0.001	ns
n3	**C20:4**	0.081±0.035	0.020±0.015	0.026±0.017	0.019±0.007	p<0.01	p<0.01	ns
n3	**C20:5**	0.124±0.052	0.037±0.014	0.030±0.009	0.026±0.012	p<0.001	p<0.001	ns
n3	**C22:5**	0.201±0.109	0.037±0.007	0.050±0.011	0.029±0.008	p<0.01	p<0.001	ns
n3	**C22:6**	0.427±0.153	0.053±0.023	0.177±0.016	0.036±0.018	p<0.001	p<0.001	p<0.05
n3	**C24:5**	0.018±0.005	0.016±0.009	0.014±0.004	0.014±0.002	ns	ns	ns
n3	**C24:6**	0.078±0.015	0.027±0.016	0.029±0.013	0.027±0.003	p<0.001	p<0.001	ns

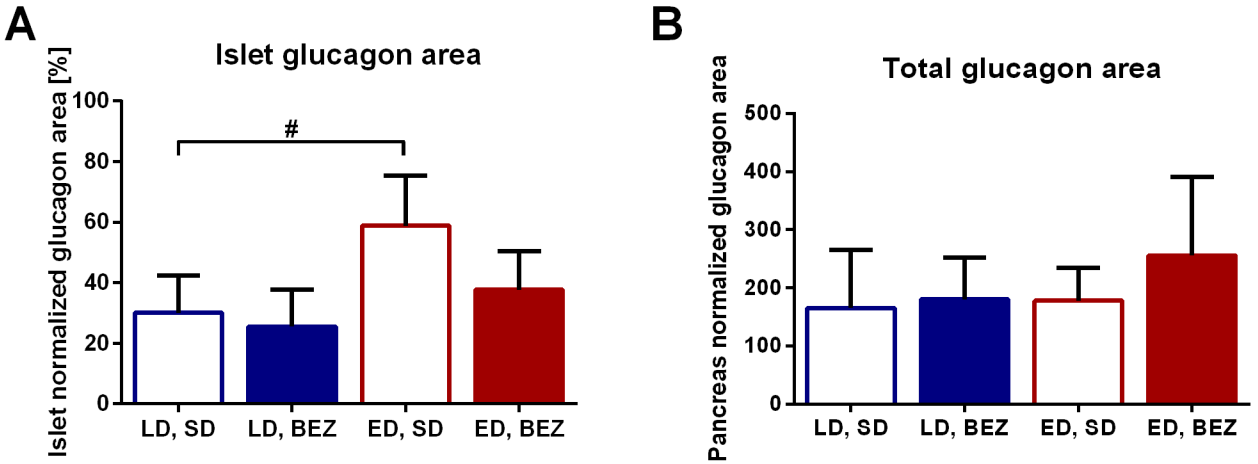
Absolute FA composition of hepatic TG fraction is shown as nmol FA/mg liver tissues. Numbers in third-sixth columns represent average values ± standard deviations. Seventh-ninth columns represent Holm-Sídáks´test calculated p values. c denotes cis FA, n-“number” denotes the position of double bounds counted from the omega carbon. n=5. The relative composition of FA in TG fraction in % is given in Figure 5C and Suppl. Fig. 5C-D.

Supplementary Table 2 Primer sequences used for real-time PCR

Symbol	Gene	5´primer	3´primer	UPL probe nr
Cs	citrate synthase	ATTCGTGGAAGAAGCACTGG	GCCATGGCTCTACTCACTGC	-
Cox19	cytochrome c oxidase assembly protein 19	GTCGACCGCAATGAACTTCG	ACATTCACCGAAGTGGTCCAG	-
Fasn	fatty acid synthase	GCTGCTGTTGGAAGTCAGC	AGTGTTCGTTCCTCGGAGTG	58
Gapdh	glyceraldehyde-3-phosphate dehydrogenase	GCCAAAAGGGTCATCATCTC	CACACCCATCACAAACATGG	29
Hadha	hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl-Coenzyme A thiolase/enoyl-Coenzyme A hydratase (trifunctional protein), alpha subunit	CTGGTCAGCAGAGCAGAAGA	ATTGGCAGTCTCAGTCGCTT	-
Ndufab1	NADH dehydrogenase (ubiquinone) 1, alpha/beta subcomplex, 1	CACCCCCACTGACGTTAGAC	ACGGAGAGCTTTTCTGGATCA	-
Rps2	ribosomal protein S2	GTGCCCAAGAAGCTCCTGAT	TGGCCTTAGCAAAGTTGCCC	-
Scd1	stearoyl-Coenzyme A desaturase 1	TTCCCTCCTGCAAGCTCTAC	CAGAGCGCTGGTCATGTAGT	34
Scd2	stearoyl-Coenzyme A desaturase 2	TGGTTTCCATGGGAGCTG	TTGATGTGCCAGCGGTACT	53
Symbol	**Gene**	**Qiagen Assay name**	**Qiagen Cat. No.**	
Cpt2	carnitine palmitoyltransferase 2	Mm_CPT2_1_SG	QT00304717	-



Suppl Figure 1



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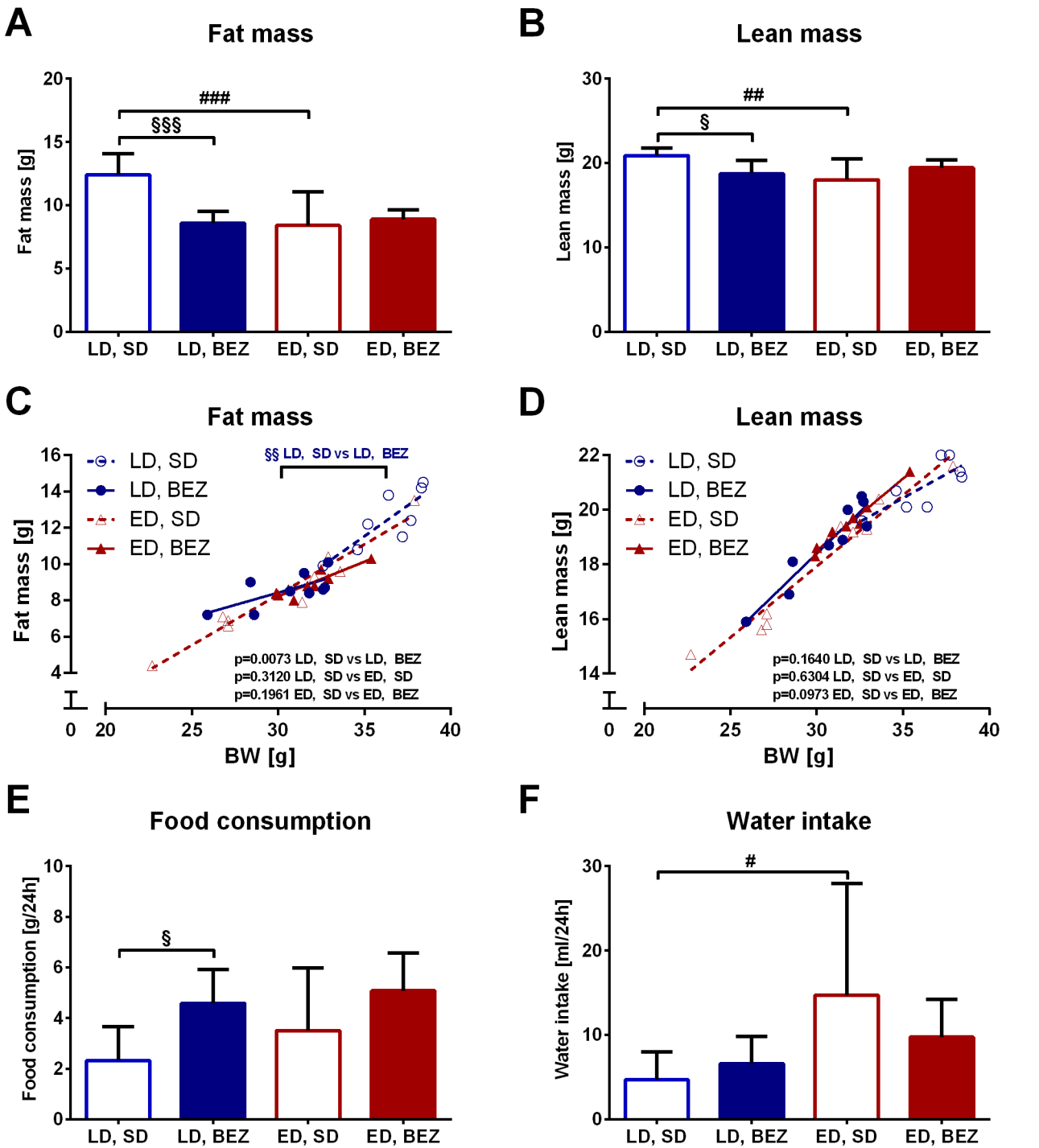

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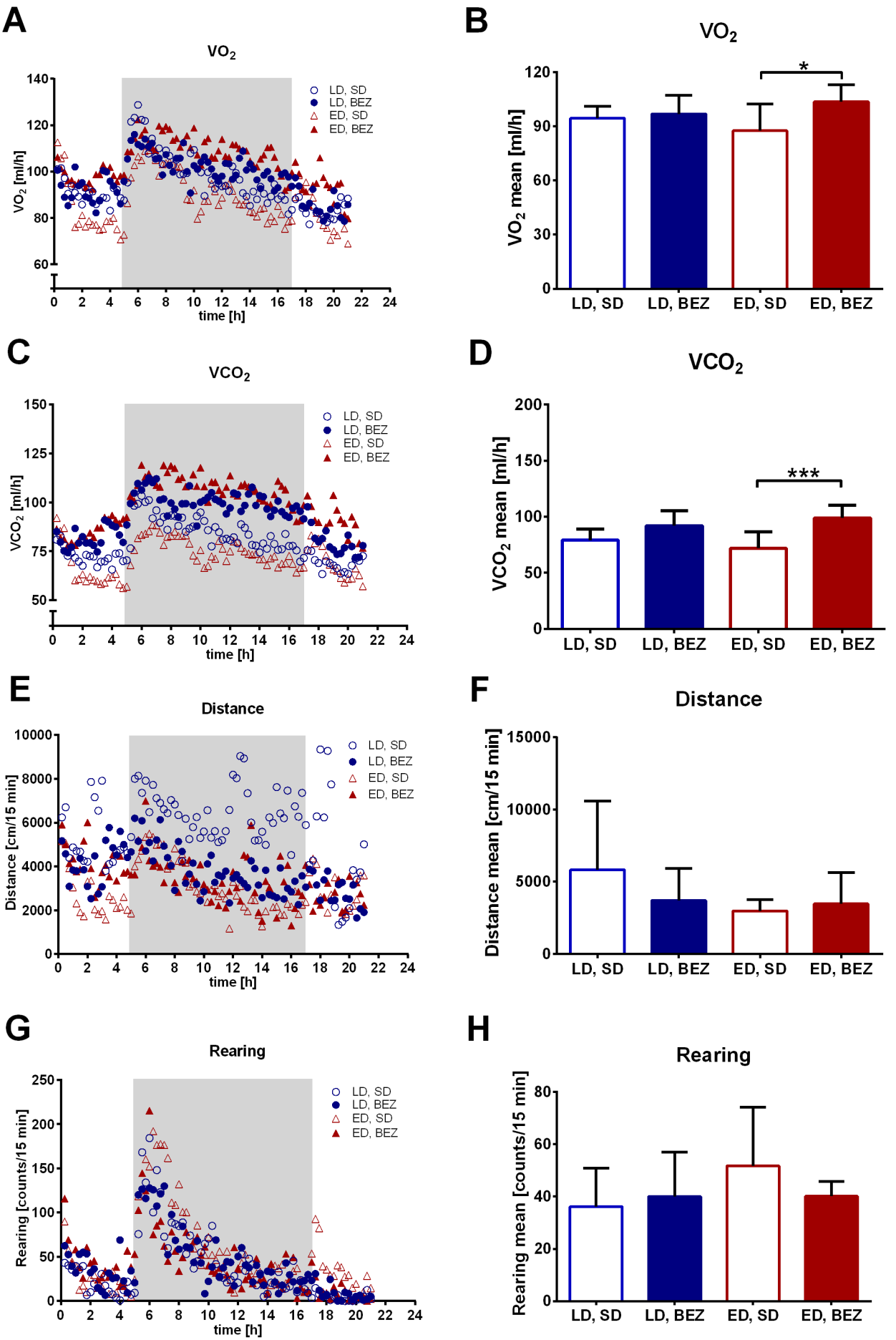

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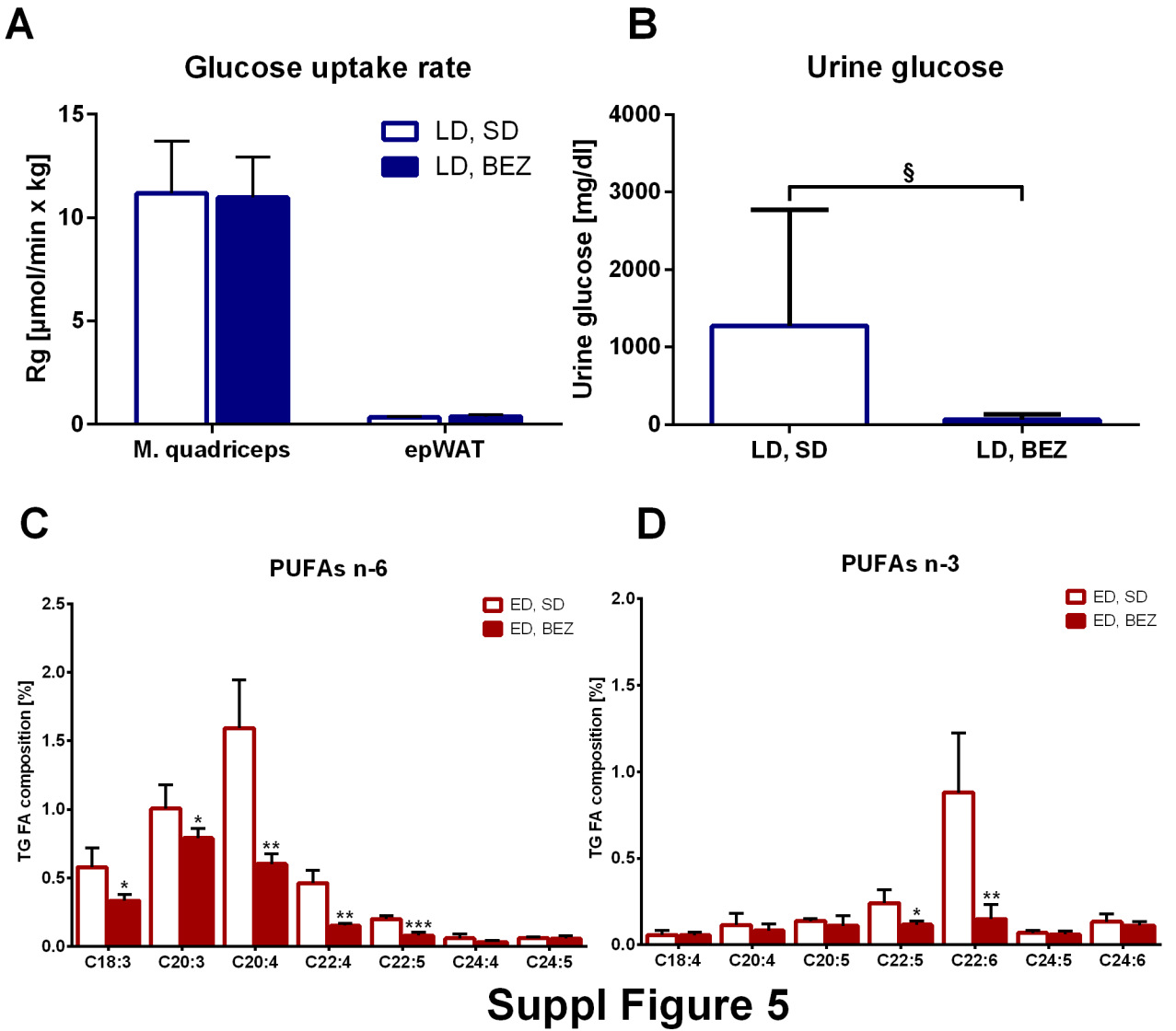

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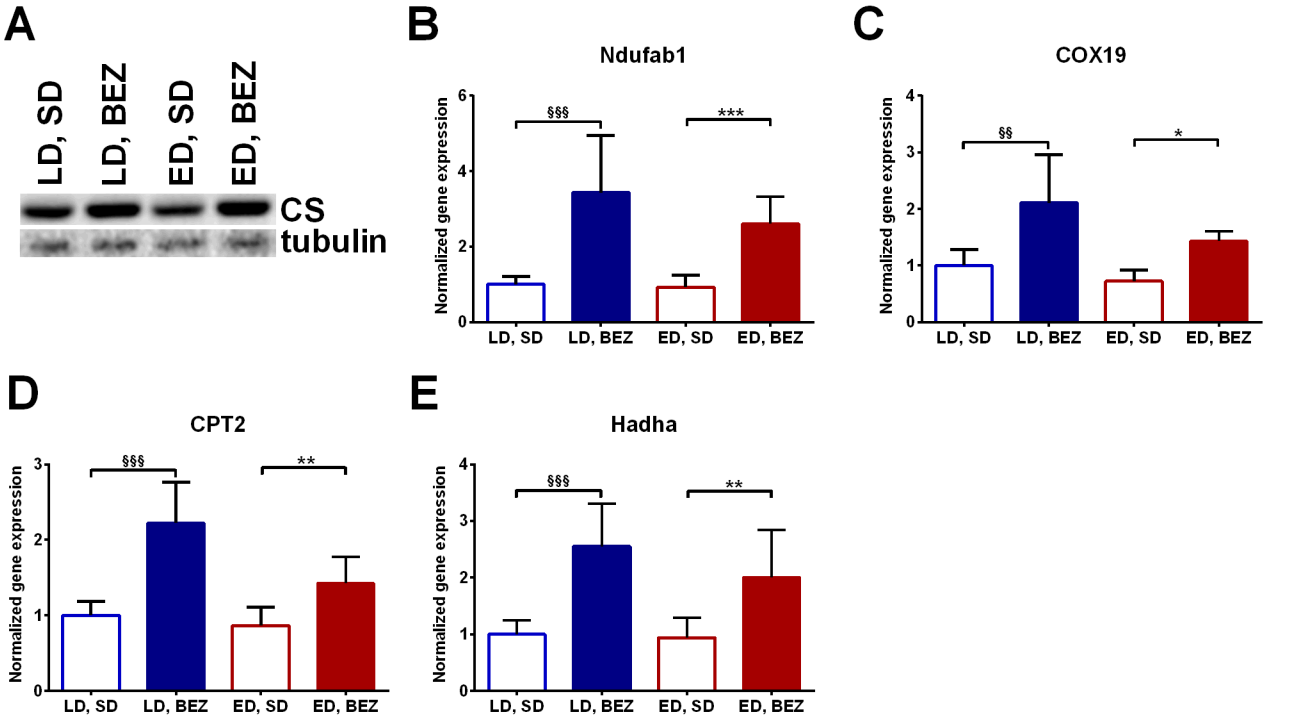

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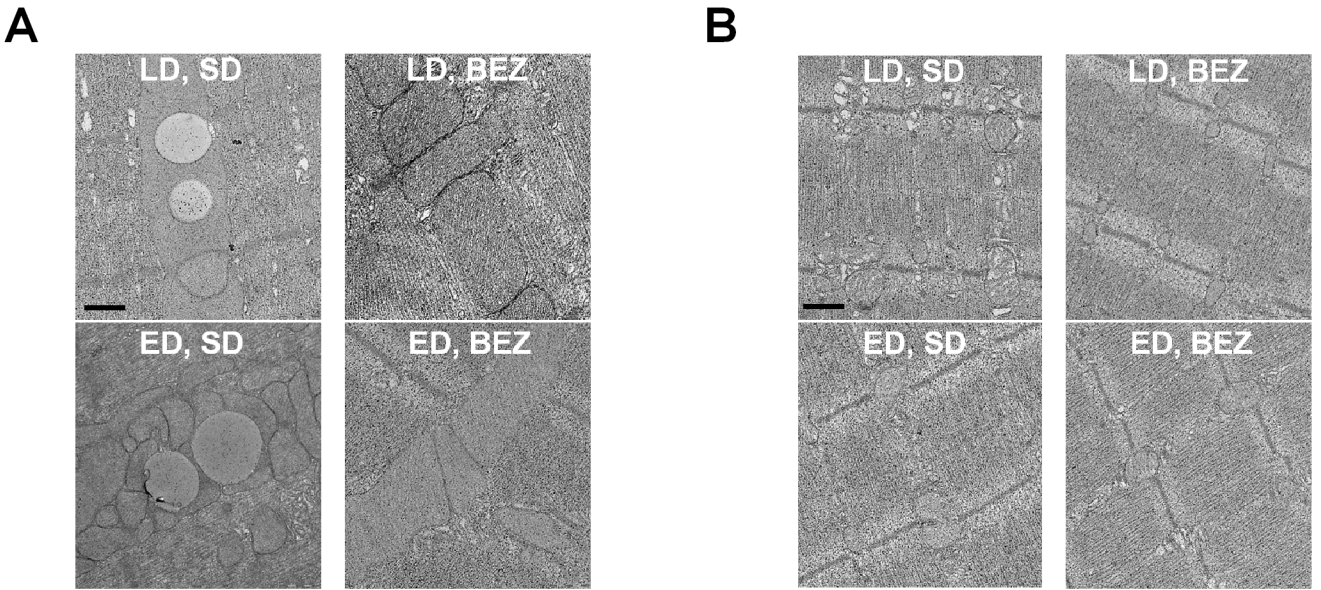

Suppl Figure 7