

SUPPLEMENTARY DATA

Impact of Perturbed Pancreatic β -cell Cholesterol Homeostasis on Adipose Tissue and Skeletal Muscle Metabolism

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Supplementary Table 1. Liver mass, liver glycogen and plasma lactate levels in β -DKO and *Abca1*fl/fl*Abcg1*fl/fl mice.

	fl/fl	β-DKO
Liver mass (g)	1.43 \pm 0.34	1.51 \pm 0.29
Liver glycogen (mg/g)	7.03 \pm 0.14	6.89 \pm 0.28
Plasma lactate (mM)	5.76 \pm 1.36	6.27 \pm 0.82

Liver Glycogen and plasma lactate levels were quantified by ELISA as described in Research Design and Methods. Values represent mean \pm SD (n=6/group).

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Supplementary Table 2. Differential protein expression in gastrocnemius muscle of β -DKO mice relative to *Abca1*fl/fl*Abcg1*fl/fl mice.

Accession	Description	P value	Fold change	Up/Down Regulated
20071000	nucleolar protein 3 (apoptosis repressor with CARD domain)	0.03	57.7	Down
12844653	acyl carrier protein, mitochondrial precursor	0.00105	29.22	Down
29244166	SH3 and cysteine-rich domain-containing protein 3	0.00205	15.25	Down
2623222	ATP synthase beta-subunit	0.03	6.66	Down
6681662	ENH3	0.00251	6	Down
31982861	carbonic anhydrase	0.02	4.75	Down
58037409	14 kDa phosphohistidine phosphatase	0.00709	4.58	Down
41054992	zinc finger CCHC domain-containing protein 5	0.000267	4.27	Down
6679937	glyceraldehyde-3-phosphate dehydrogenase	0.04	4.1	Down
6671762	creatine kinase M-type	0.02	3.95	Down
26345188	peroxiredoxin-6	0.00000926	3.78	Down
26340966	alpha-fetoprotein	0.01	3.76	Down
148709256	PDZ and LIM domain 7	0.05	3.36	Down
5882218	histidine-rich Ca ²⁺ binding protein	0.000264	3.12	Down
26328977	neurofibromin	0.00791	3.1	Down
6679078	nucleoside diphosphate kinase B	0.02	3.05	Down
45774102	stretch-responsive fibronectin protein type 3	0.01	2.98	Down
148665221	alpha-2-HS-glycoprotein	0.00968	2.6	Down
31712014	carboxymethylenebutenolidase homolog	0.01	2.46	Down
475756	microtubule-associated protein 4	0.02	2.36	Down
200065	neuroleukin	0.00243	2.29	Down
313103	skelemin	0.04	2.17	Down
148703606	PDZ and LIN domain 3	0.0019	2.14	Down
84872217	LIM domain-binding protein 3	0.00448	2.06	Down
16930823	proline synthase co-transcribed bacterial homolog protein	0.00736	2.05	Down
359718915	E3 ubiquitin-protein ligase C12orf51 homolog	0.01	19.61	Up
51593432	Ptms protein	0.04	15.28	Up
23821025	CAP-Gly domain-containing linker protein 1	0.00249	10.96	Up
575936	fructose 1,6-bisphosphatase	0.04	9.48	Up
2078284	amyloid beta-peptide binding protein	0.00518	7.45	Up
12832367	electron transferring flavoprotein, beta polypeptide	0.03	6.02	Up

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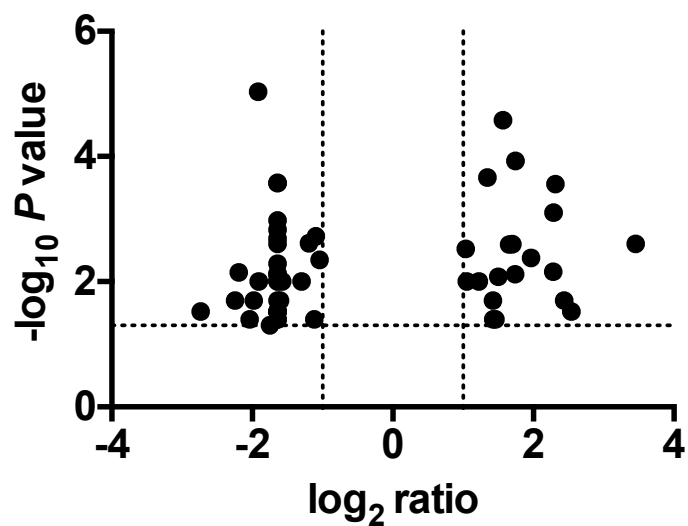
13385042	protein FAM136A	0.03	5.82	Up
13385260	acyl-coenzyme A thioesterase 13	0.02	5.41	Up
31980767	parvalbumin alpha	0.000277	4.97	Up
9256624	phosphoglycerate mutase 2	0.000793	4.88	Up
74198620	cathepsin D	0.00692	4.86	Up
7657558	SH3 domain-binding glutamic acid-rich protein	0.00148	3.97	Up
31982520	long-chain specific acyl-CoA dehydrogenase, mitochondrial precursor	0.00418	3.91	Up
1160331	dbpA murine homologue	0.000118	3.35	Up
26325878	CAP-Gly domain-containing linker protein 1	0.00761	3.34	Up
673431	precursor adipsin	0.03	3.27	Up
6680806	bisphosphoglycerate mutase	0.00254	3.25	Up
21450129	acetyl-CoA acetyltransferase, mitochondrial precursor	0.00256	3.15	Up
53581	annexin A6	0.0000265	2.96	Up
202423	phosphoglycerate kinase	0.00841	2.83	Up
359807367	pyruvate kinase	0.04	2.75	Up
12846616	beta-globin	0.04	2.69	Up
12832230	ATP synthase subunit delta, mitochondrial precursor	0.02	2.68	Up
148690894	histidine rich calcium binding protein	0.000217	2.54	Up
148700389	Hspd1 protein	0.03	2.46	Up
21704140	3-hydroxyisobutyrate dehydrogenase, mitochondrial precursor	0.01	2.34	Up
59958370	heat shock protein beta-6	0.01	2.07	Up
6680309	10 kDa heat shock protein, mitochondrial	0.003	2.05	Up

Gastrocnemius muscles from 16 week old β -DKO mice and *Abca1fl/fl/Abcg1fl/fl* mice were homogenized. Proteins were precipitated with acetone, digested with trypsin and identified by mass spectrometry. A 2-fold change in expression and $P < 0.05$ was considered significant.

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Supplementary Figure 1. Volcano plot showing gastrocnemius proteins with significantly altered expression between β -DKO and *Abca1*fl/fl*Abcg1*fl/fl mice.

Proteins were identified by mass spectrometry. A 2-fold change in expression and $P < 0.05$ was considered significant. Identities of proteins are presented in Supplementary Table 1.



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Supplementary Figure 2. β -DKO mice do not develop insulin resistance after pump implantation. (A) Insulin tolerance and (B) glucose tolerance test were performed in mice 24 h after pump removal (to eliminate the impact of exogenous insulin) (n=5/group). No change in insulin tolerance was observed, indicating that insulin supplementation did not result in insulin resistance. A significant improvement in glucose tolerance was observed in the insulin-supplemented mice, most likely due to increased skeletal muscle mass.

