SUPPLEMENTARY FIGURE LEGENDS

Supplementary FigureS1. Characterization of mouse *Sod2*$^{+/-}$ and *Sod2*$^{+/+}$ embryonic fibroblast primary cell cultures. (a) The levels of MnSOD, UCP1 and UCP2 proteins in the primary cells obtained from the *Sod2*$^{+/-}$ and *Sod2*$^{+/+}$ mice were confirmed and are shown in comparison to corresponding mouse skin tissues (Figure 1). (b,c) ATP and lactate productions in the cells were measured.

Supplementary Table S2. MnSOD deficiency leads to lipid utilization.

Supplementary Figure S3. Alterations in glycolytic metabolism in lipid-depleted cells. The *Sod2*$^{+/-}$ and *Sod2*$^{+/+}$ primary cells were cultured in DMEM and lipid-reduced DMEM media. (a) The mRNA level of GAPDH was quantified by qRT-PCR normalized with average images of CuZnSOD and β-actin. (b) The mRNA level of lactate dehydrogenase A (LDH-A) was quantified by qRT-PCR. (c) The protein levels in the cells were measured.

Supplementary data from the experimental procedures

qRT-PCR, Western blots and ATP production

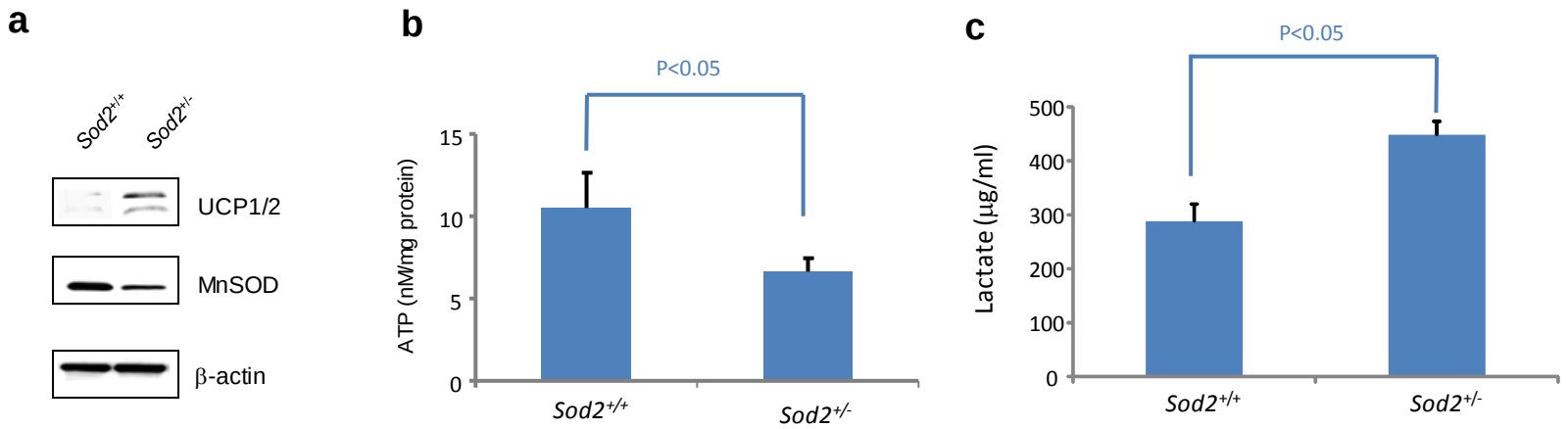
Sod2$^{+/-}$ and *Sod2*$^{+/+}$ embryonic fibroblast primary cells were cultured in DMEM and lipid-reduced DMEM media. Total cellular mRNA and proteins were extracted and subjected to qRT-PCR and Western blots to quantify the levels of mRNA and proteins using gene-specific primer sets and antibodies. CuZnSOD and β-actin were used as internal controls. 100 μg cell extracts were used to measure ATP production as described in the paper.

Metabolism analysis using mouse skin tissues

The skin tissues from 6 mice for each genotype (*Sod2*$^{+/+}$ and *Sod2*$^{+/-}$) were prepared as described previously.[10] The tissues were provided to Metabolomics Fiehn Laboratory for analysis of metabolism using a developed metabolic array.

Supplementary data

S1

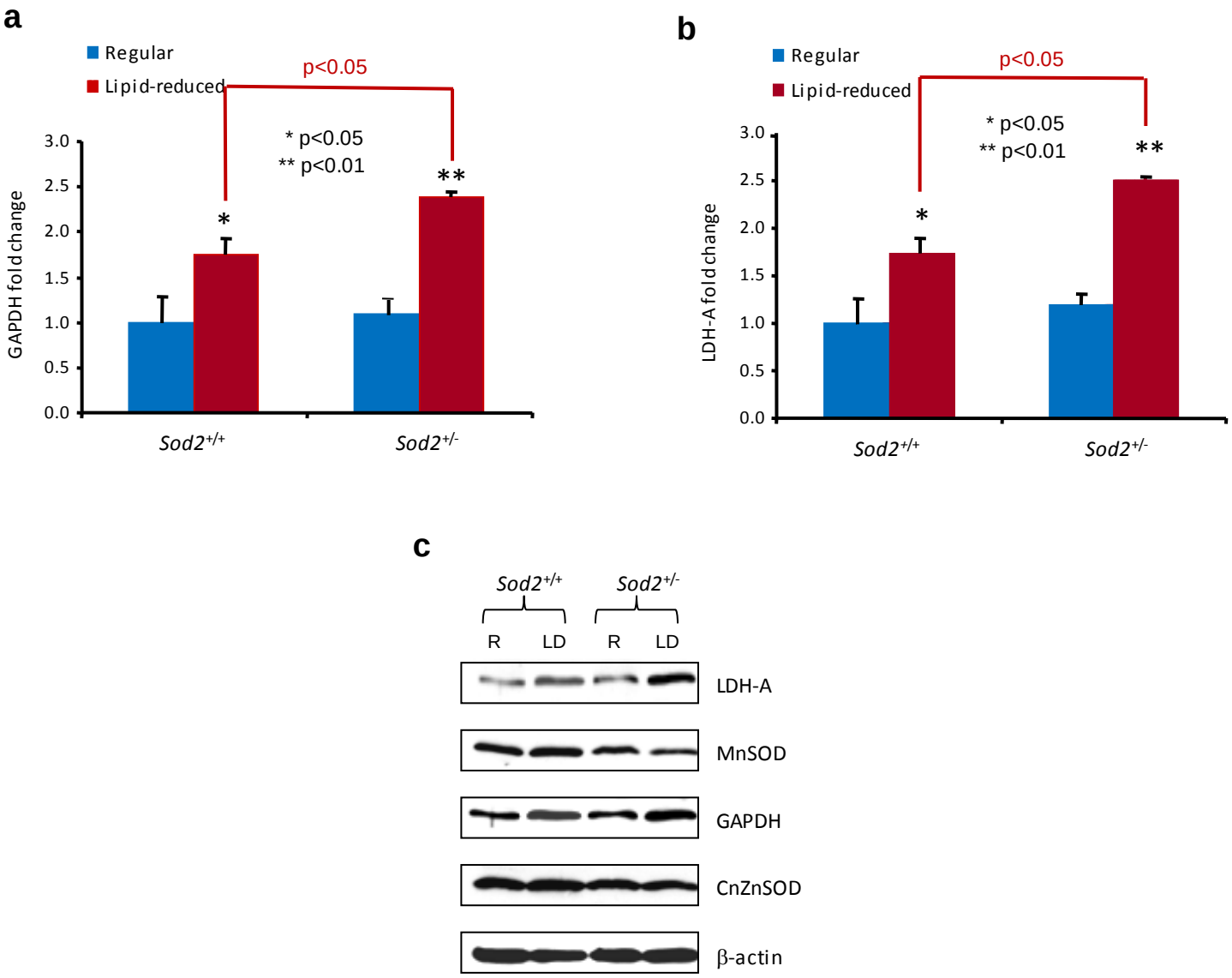


S2

Metabolism comparison in skin tissues (*Sod2* $^{+/-}$ vs. *Sod2* $^{+/+}$)

Group	Pathway	Biochemical name	*SOD2*$^{+/-}$ vs. *SOD2*$^{+/+}$	P-value
Amino acid	Valine, Leucine and isoleucine metabolism	4-methyl -2-oxopentanoate	0.9	0.0387
	Urea cycle; arginine proline, metabolism	urea	0.79	0.0262
	Glutathione metabolism	ophthalmate	0.86	0.0512
Energy	Oxidative Phosphorylation	methylphosphate	0.41	0.0043
Lipid	Essential fatty acid	dihomo-linolenate (20:3n3 or n6)	0.65	0.0494
		docosahexaenoate (DHA; 22:6n3)		
	Long chain fatty acid	palmitate (16:0)	0.71	0.0482
		margarate (17:0)		
		10-heptadecenoate (17:1n7)		
		oleate (18:1n9)		
		linoleate (18:2n6)		
		eicosenoate (20:1n9 or 11)		
Nucleotide	Pruine metabolism; (hypo)xanthine/ inosine	Inosine	0.4	0.0138
Xenobiotics	Chemical	glycerol 2-phosphate	0.45	0.0035

S3


a
Regular
Lipid-reduced
p<0.05
* p<0.05
** p<0.01
GAPDH fold change
3.0
2.5
2.0
1.5
1.0
0.5
0.0
*
**
Sod2+/+
Sod2+/-
b
Regular
Lipid-reduced
p<0.05
* p<0.05
** p<0.01
LDH-A fold change
3.0
2.5
2.0
1.5
1.0
0.5
0.0
*
**
Sod2+/+
Sod2+/-
c
Sod2+/+
Sod2+/-
R
LD
R
LD
LDH-A
MnSOD
GAPDH
CnZnSOD
β-actin