Deletion of RAGE fails to prevent hepatosteatosis in obese mice due to impairment of other AGEs receptors and detoxifying systems.

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Supplementary Table 1. Primers for RT-PCR

PRIMER	FORWARD	REVERSE
RAGE	5'-GTCCGAGTCTACCAGATTCCT -3'	5'-GAAGTTTCCCATCTAAGTGCC-3'
AGER-1	5'-ACCTTCAAGACCGCAGATGA-3'	5'-CACGTTGATGTTGCCTCCAA-3'
Gal-3	5'-CCCGCATGCTGATCACAATC-3'	5'-GGGGTTAAAGTGGAAGGCAA-3'
Aldose reductase	5'-CGTGATACCTAGTGACACCGA-3'	5'-GCCAGGTTTGTTCAAGATCCT-3'
Glo-1	5'-CCCTGCTATGAAGTTCTCGCTC-3'	5'-GAGCTCAAGGGTGGCTTTTCT-3'
Nrf2	5'-TTGGCAGAGACATTCCCAT-3'	5'-GCTGCCACCGTCACTGGG-3'

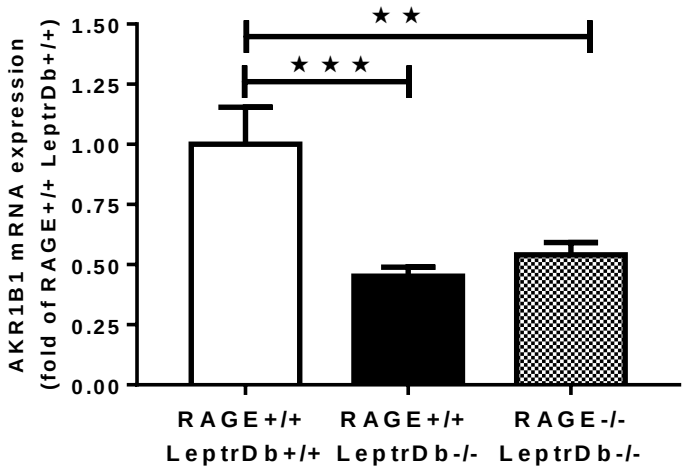
Supplementary Table 2. Primary antibodies for western blotting analysis.

ANTIBODIES	COMPANY	CAT. NO.
Mouse monoclonal anti-RAGE	Santa Cruz Biotechnology, Inc., Dallas, TX, USA	sc-365154
Rabbit Polyclonal anti-SREBP1c	Abcam	ab44153
Mouse Monoclonal anti-α-Tubulin	Abcam	ab7291
Mouse Monoclonal anti-Gal-3	Affinity BioReagents, Golden, CO, USA	MA1-940
Rabbit Polyclonal anti-ACC	Cell Signaling Technology, Danvers, MA, USA	3662
Rabbit Monoclonal anti-NLRP3	Epitomics, Burlingame, CA, USA	3560-1
Rabbit Polyclonal anti-Glo-1	Genetex, Irvine, CA, USA	GTX105792
Mouse Monoclonal anti-β-Actin	Santa Cruz Biotechnology	sc-47778
Rabbit Polyclonal anti-Caspase 1 (p10)	Santa Cruz Biotechnology	sc-514
Mouse Monoclonal anti-FASN	Santa Cruz Biotechnology	sc-55580
Rabbit Polyclonal anti-Histone H3	Santa Cruz Biotechnology	sc-10809
Mouse Monoclonal anti-IL-1β	Santa Cruz Biotechnology	sc-52012
Mouse Monoclonal anti-MyD88	Santa Cruz Biotechnology	sc-74532
Mouse Monoclonal anti-NFkB-p65	Santa Cruz Biotechnology.	sc-8008
Mouse Monoclonal anti-OST48 (AGER1)	Santa Cruz Biotechnology	sc-74408
Rabbit Polyclonal anti-Nrf2	Thermo Fisher Scientific, Waltham, MA, USA	PA5-27882

Supplementary Table 3. Body weight and cytokines plasma levels in control (RAGE+/+ LeptrDb+/+), obese (RAGE+/+ LeptrDb-/-), and RAGE KO obese (RAGE-/- LeptrDb-/-) mice. Data are means ± SEM of 5-10 animals per group. Statistical significance: *P<0,05 vs RAGE+/+ LeptrDb+/+; §P<0,05 vs RAGE+/+ LeptrDb-/-.

	RAGE+/+ LeptrDb+/+	RAGE+/+ LeptrDb-/-	RAGE-/- LeptrDb-/-
Body weight (g)	24.1 ± 0.6	35.0 ± 5.0	39.5 ± 5.0
IL-1β (pg/ml)	2.4 ± 0.9	8.0 ± 1.3*	2.4 ± 1.0§
IFN-γ (pg/ml)	0.9 ± 0.1	2.1 ± 0.3*	1.1 ± 0.2§
TNF-α (pg/ml)	1.0 ± 0.4	2.3 ± 0.6*	0.6 ± 0.7§

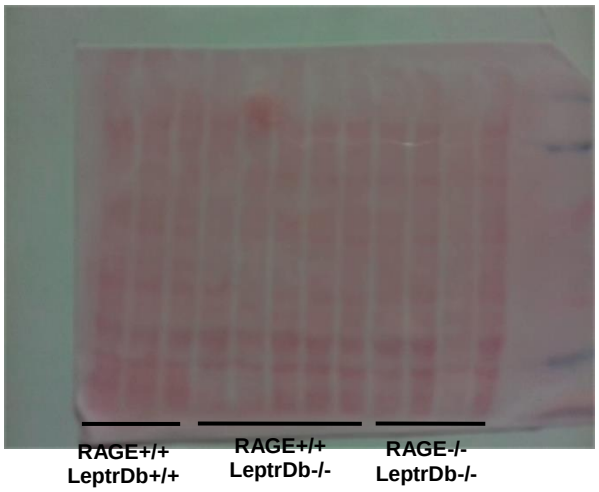
Supplementary Figure 1. PCR analysis for gene expression of the AGEs detoxyfying enzyme aldose reductase in liver mRNA extracts. Data are means ± s.e.m. of 4-6 animals per group. Statistical significance: **P<0,01; ***P<0,001.

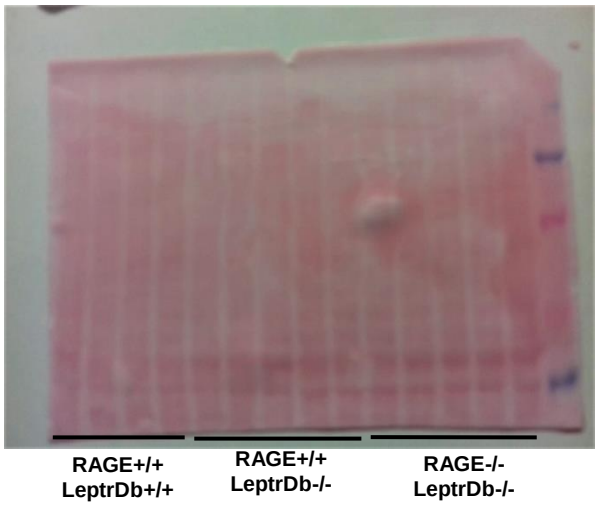


Supporting information

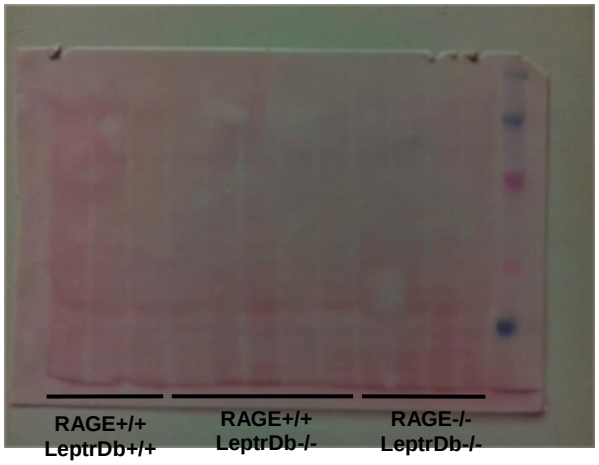
Ponceau S staining

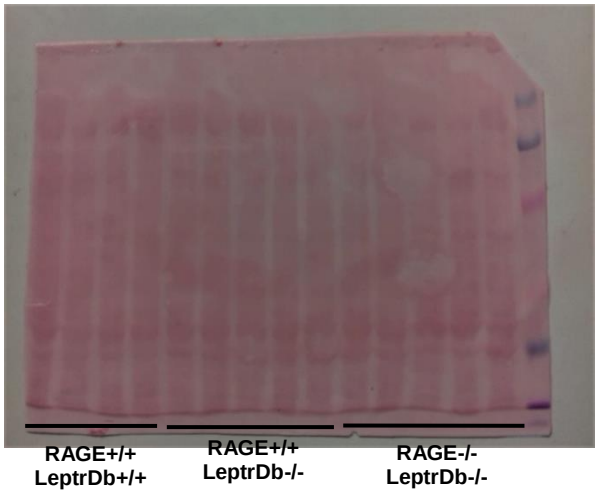
Total extracts





Cytosolic extracts

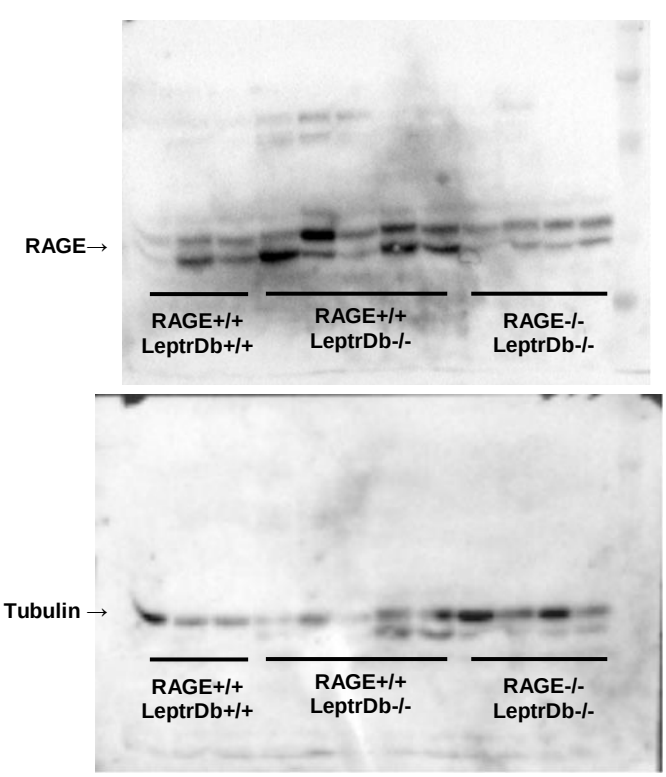




Original blots for western blotting figures

Figure 1.

A



E

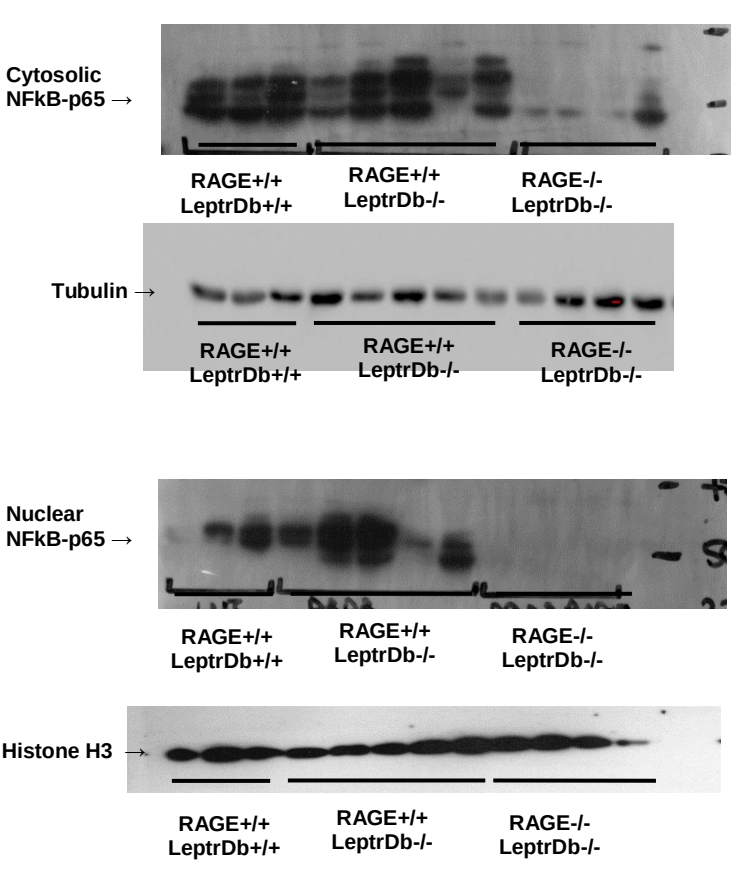
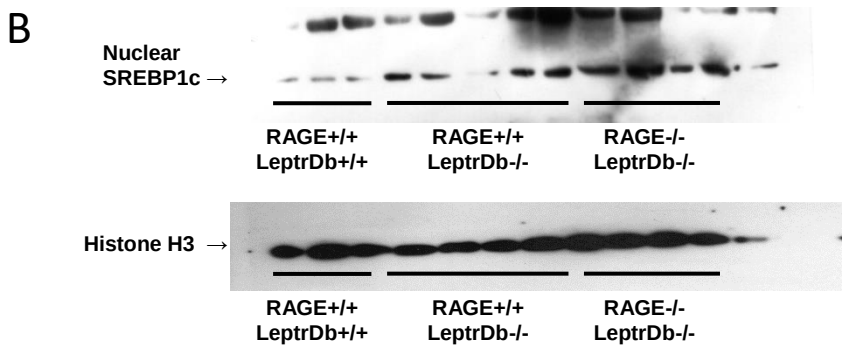
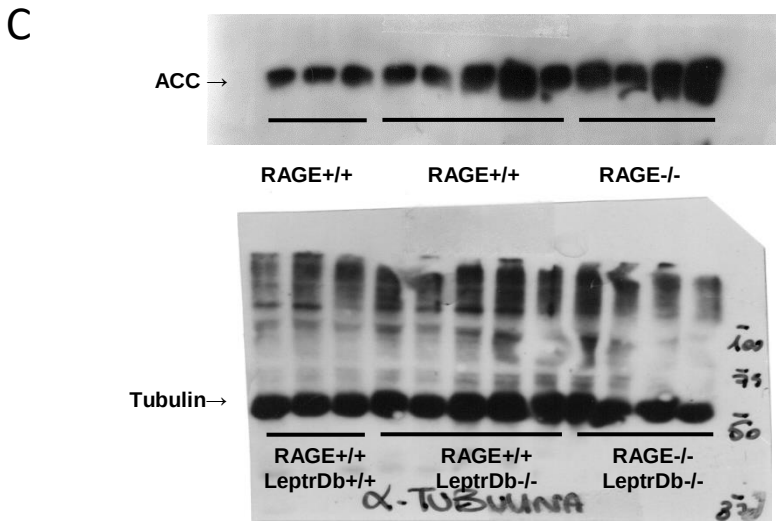


Figure 2.


B
Nuclear
SREBP1c →
RAGE+/+
LeptrDb+/+
RAGE+/+
LeptrDb-/-
RAGE-/-
LeptrDb-/-
Histone H3 →
RAGE+/+
LeptrDb+/+
RAGE+/+
LeptrDb-/-
RAGE-/-
LeptrDb-/-


C
ACC →
RAGE+/+
RAGE+/+
RAGE-/-
Tubulin→
RAGE+/+
LeptrDb+/+
RAGE+/+
LeptrDb-/-
RAGE-/-
LeptrDb-/-
α-TUBULINA

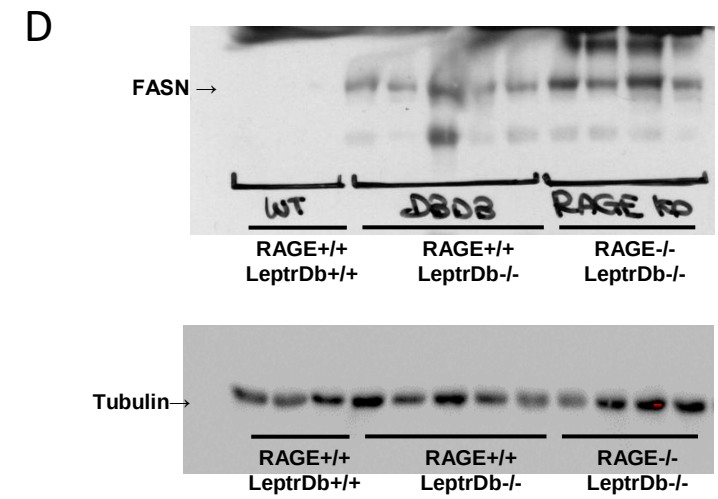
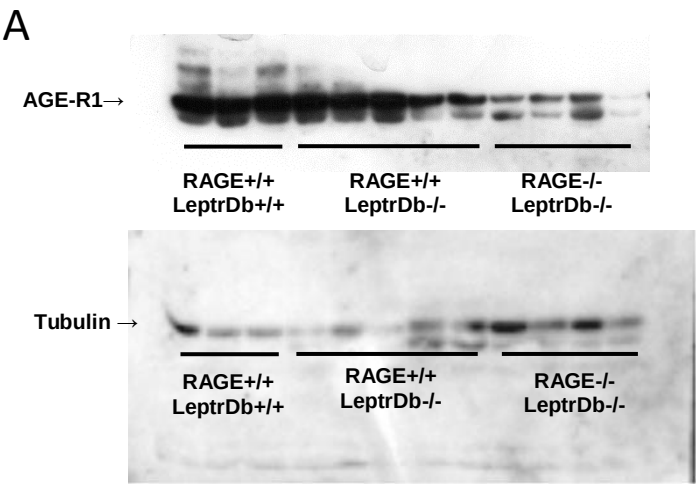

D
FASN →
WT
DBDB
RAGE KO
RAGE+/+
LeptrDb+/+
RAGE+/+
LeptrDb-/-
RAGE-/-
LeptrDb-/-
Tubulin→
RAGE+/+
LeptrDb+/+
RAGE+/+
LeptrDb-/-
RAGE-/-
LeptrDb-/-

Figure 3.

A


AGE-R1→
RAGE+/+ LeptrDb+/+
RAGE+/+ LeptrDb-/-
RAGE-/- LeptrDb-/-
Tubulin →
RAGE+/+ LeptrDb+/+
RAGE+/+ LeptrDb-/-
RAGE-/- LeptrDb-/-

B

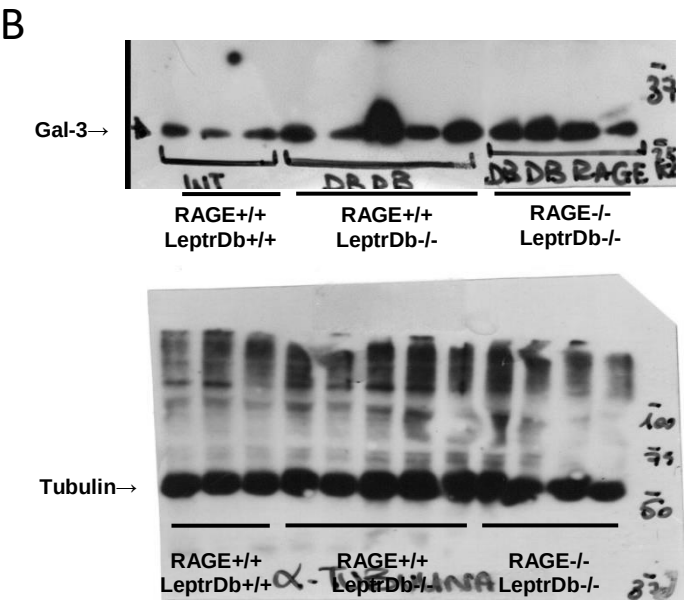
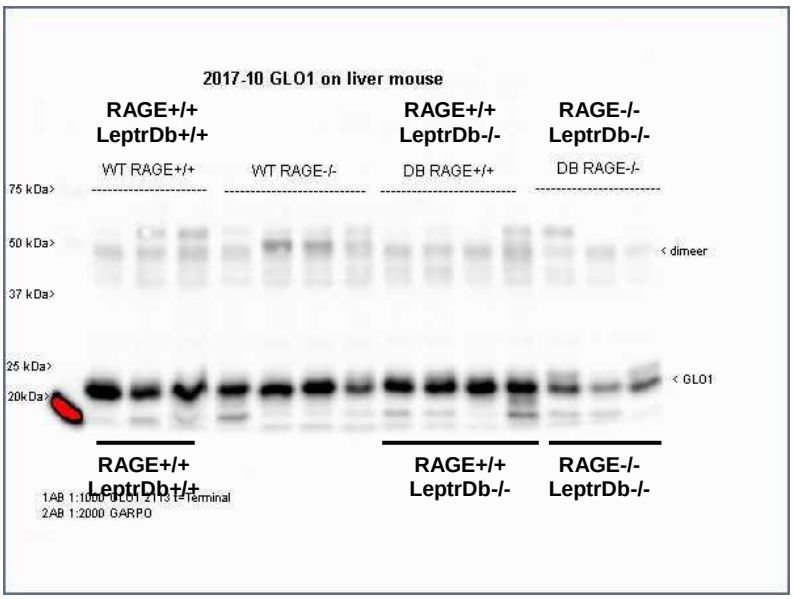
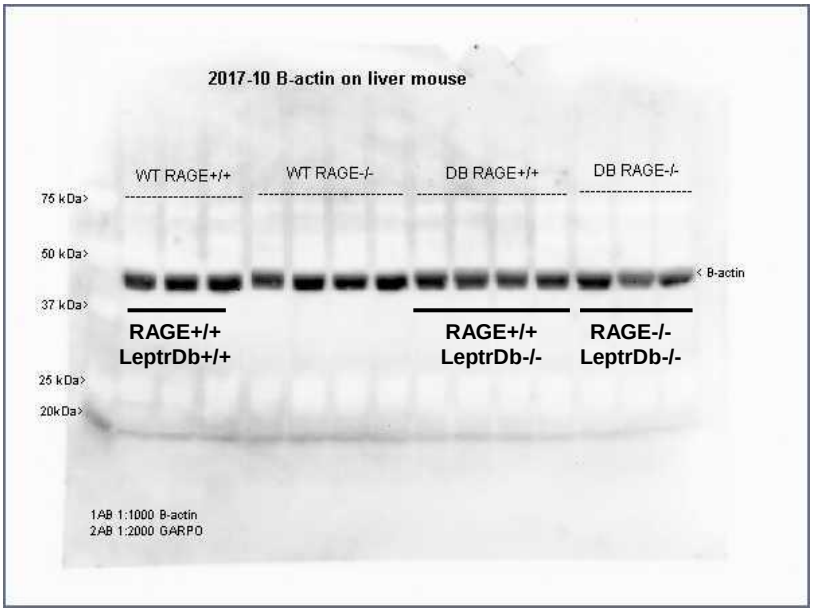

Gal-3→
WT
DB DB
DB DB RAGE
RAGE+/+ LeptrDb+/+
RAGE+/+ LeptrDb-/-
RAGE-/- LeptrDb-/-
Tubulin→
RAGE+/+ LeptrDb+/+
RAGE+/+ LeptrDb-/-
RAGE-/- LeptrDb-/-

Figure 4.



Glo-1 dimer 42 kDa →

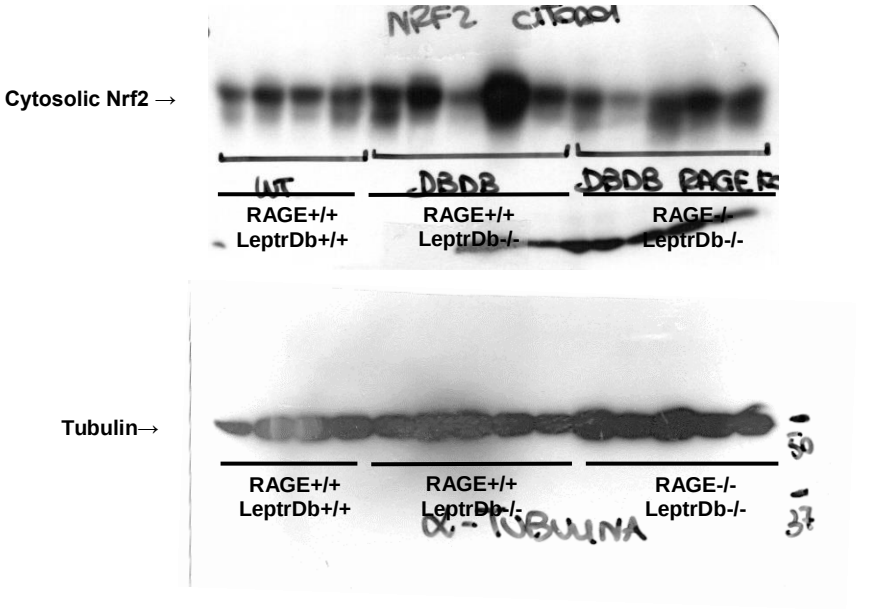
Glo-1 monomer 21 kDa →

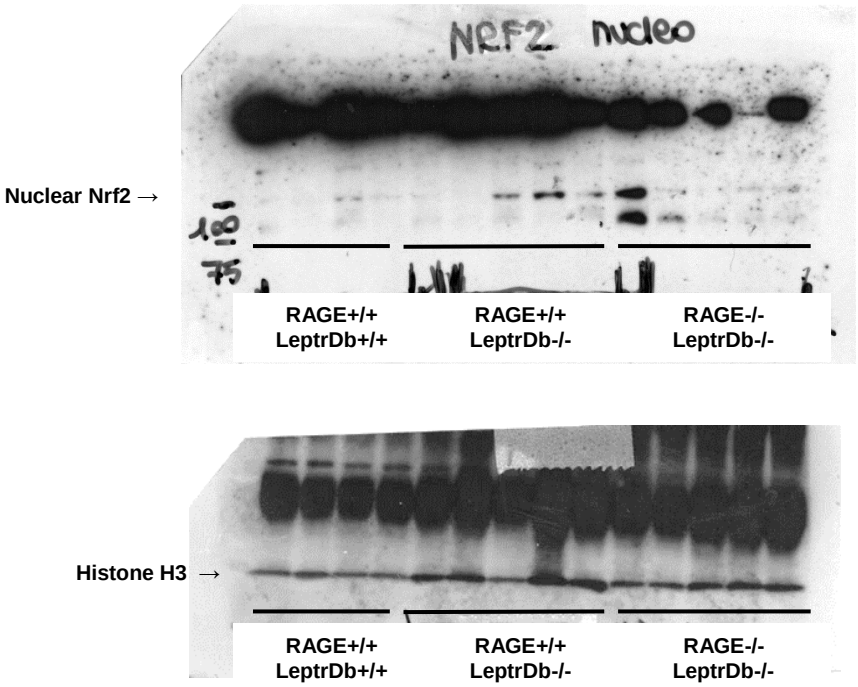


β-actin →

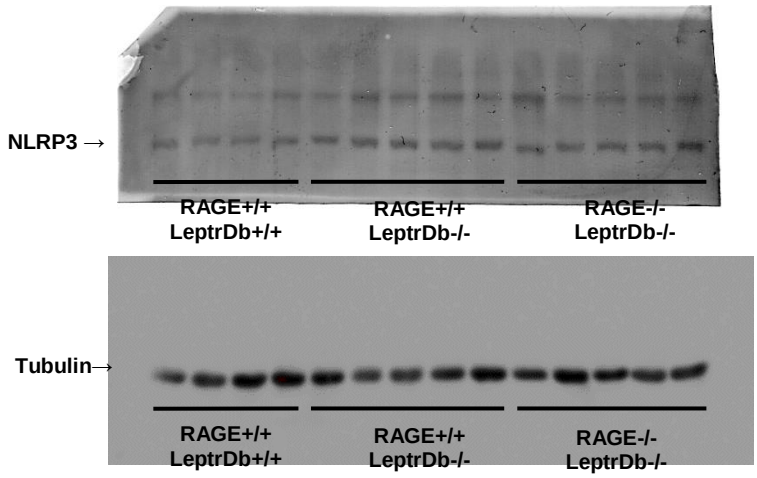
Figure 5.

B

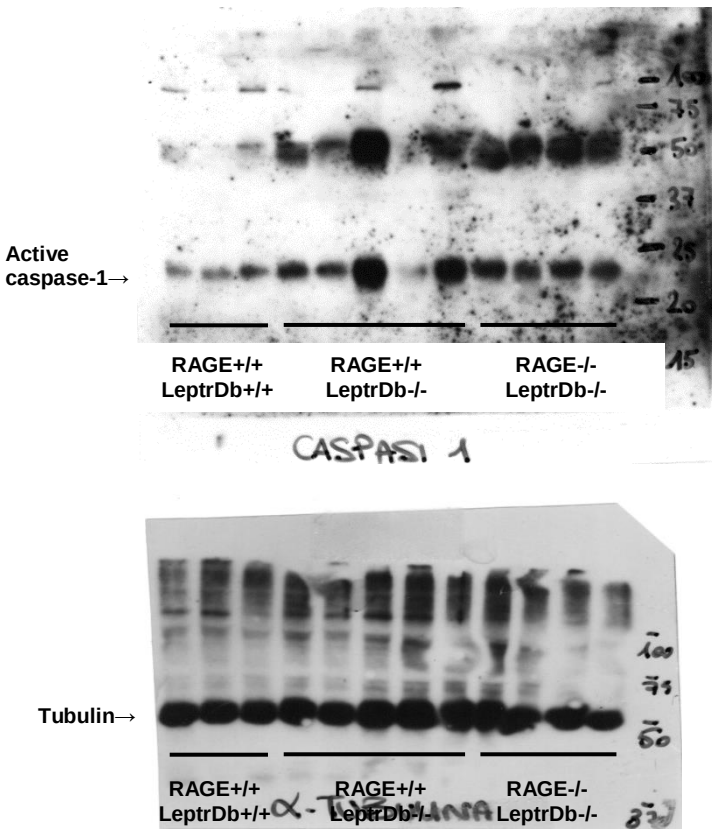

Cytosolic Nrf2 →
NRF2 CITOSOL
WT
DBDB
DBDB RAGE
RAGE+/+
LeptrDb+/+
RAGE+/+
LeptrDb-/-
RAGE-/-
LeptrDb-/-
Tubulin→
RAGE+/+
LeptrDb+/+
RAGE+/+
LeptrDb-/-
RAGE-/-
LeptrDb-/-
50
37


Nuclear Nrf2 →
NRF2 nucleo
100
75
RAGE+/+
LeptrDb+/+
RAGE+/+
LeptrDb-/-
RAGE-/-
LeptrDb-/-
Histone H3 →
RAGE+/+
LeptrDb+/+
RAGE+/+
LeptrDb-/-
RAGE-/-
LeptrDb-/-

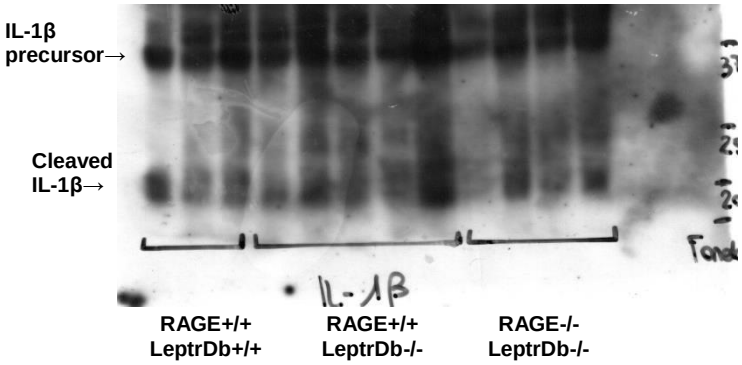
C


NLRP3 →
RAGE+/+ LeptrDb+/+
RAGE+/+ LeptrDb-/-
RAGE-/- LeptrDb-/-
Tubulin→
RAGE+/+ LeptrDb+/+
RAGE+/+ LeptrDb-/-
RAGE-/- LeptrDb-/-

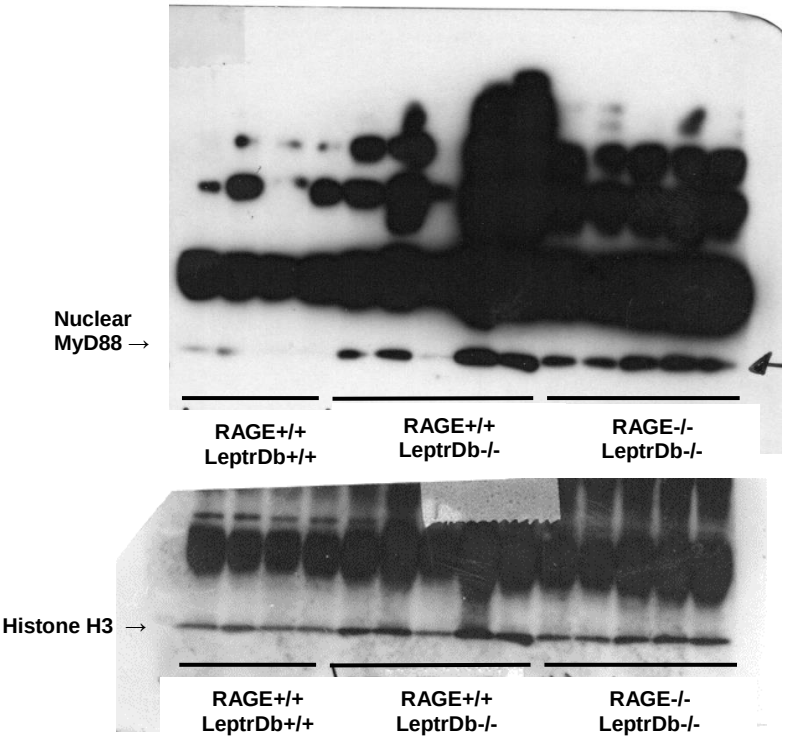
D


Active caspase-1→
RAGE+/+ LeptrDb+/+
RAGE+/+ LeptrDb-/-
RAGE-/- LeptrDb-/-
CASPASI 1
Tubulin→
RAGE+/+ LeptrDb+/+
RAGE+/+ LeptrDb-/-
RAGE-/- LeptrDb-/-

E


IL-1β
precursor→
Cleaved
IL-1β→
IL-1β
RAGE+/+
LeptrDb+/+
RAGE+/+
LeptrDb-/-
RAGE-/-
LeptrDb-/-

F


Nuclear
MyD88 →
RAGE+/+
LeptrDb+/+
RAGE+/+
LeptrDb-/-
RAGE-/-
LeptrDb-/-
Histone H3 →
RAGE+/+
LeptrDb+/+
RAGE+/+
LeptrDb-/-
RAGE-/-
LeptrDb-/-