Supplemental Table S1. Primer sequences used for quantitative PCR.

Gene	Primer	Sequence 5'-3'
Ppara	*FW*	ATG CCA GTA CTG CCG TTT TC
	RV	GGC CTT GAC CTT GTT CAT GT
Cpt1	*FW*	GAG ACT TCC AAC GCA TGA CA
	RV	ATG GGT TGG GGT GAT GTA GA
Acox1	*FW*	TAA CTT CCT CAC TCG AAG CCA
	RV	AGT TCC ATG ACC CAT CTC TGT C
Txnip	*FW*	TCT TTT GAG GTG GTC TTC AAC G
	RV	GCT TTG ACT CGG GTA ACT TCA CA
Ucp2	*FW*	ATG GTT GGT TTC AAG GCC ACA
	RV	CGG TAT CCA GAG GGA AAG TGA T
Ucp3	*FW*	CCG ATT TCA AGC CAT GAT ACG C
	RV	CCT GGC GAT GGT TCT GTA GG
Nox4	*FW*	GAA GGG GTT AAA CAC CTC TGC
	RV	ATG CTC TGC TTA AAC ACA ATC CT
Tfam	*FW*	ATT CCG AAG TGT TTT TCC AGC A
	RV	TCT GAA AGT TTT GCA TCT GGG T
Hprt	*FW*	AGT CCC AGC GTC GTG ATT AG
	RV	TTT CCA AAT CCT CGG CAT AAT GA
B2M	*FW*	CCC CAC TGA GAC TGA TAC ATA CG
	RV	CGA TCC CAG TAG ACG GTC TTG
12S	*FW*	ACC GCG GTC ATA CGA TTA AC
	RV	CCC AGT TTG GGT CTT AGC TG
Cox1	*FW*	GCC CCA GAT ATA GCA TTC CC
	RV	GTT CAT CCT GTT CCT GCT CC

Supplemental Table S2. Plasma oxylipin concentration [nM].

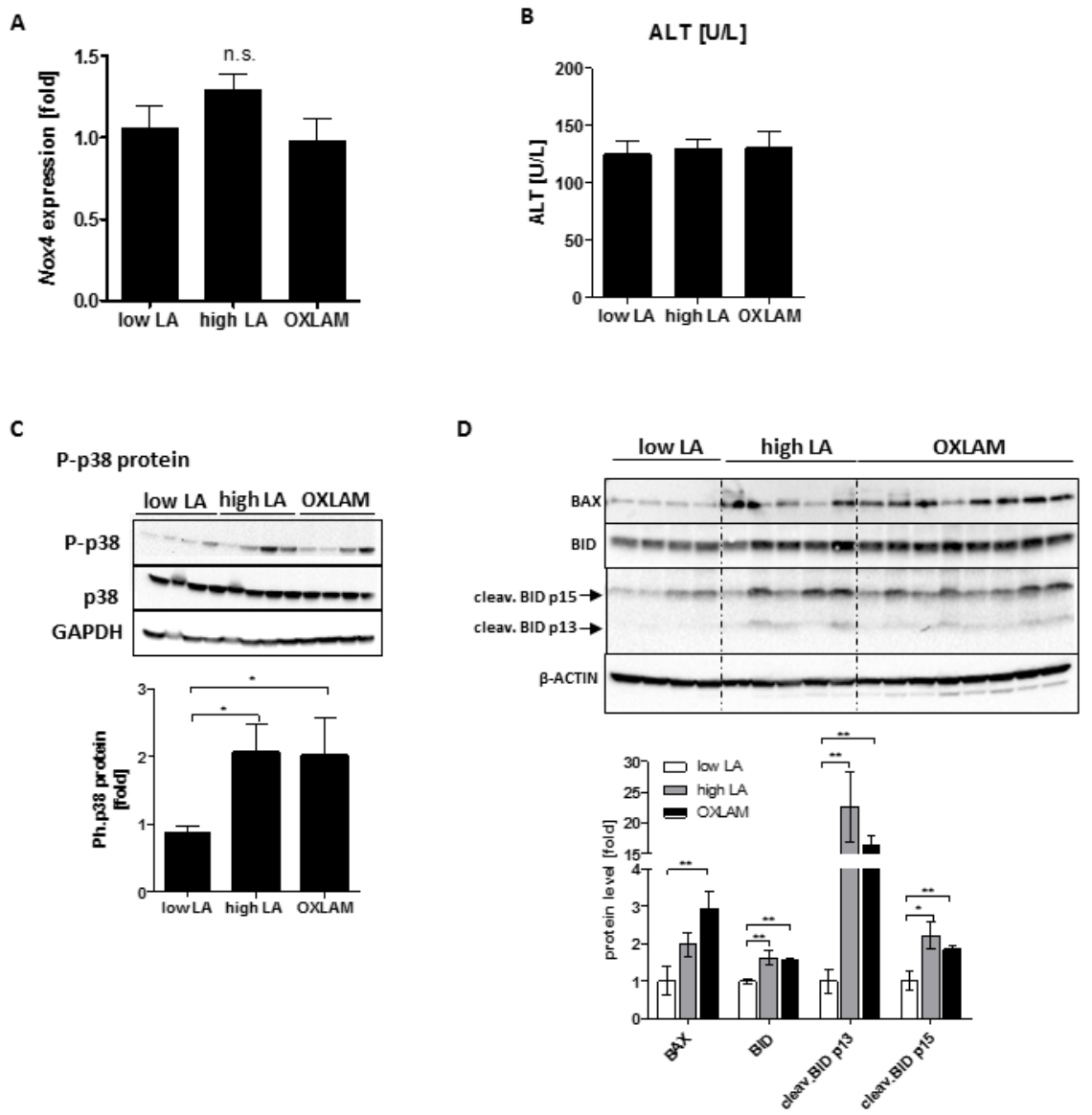
	low LA			high LA			OXLAMs		
metabolites [in nM]	**mean**	**SEM**	**N**	**Mean**	**SEM**	**N**	**Mean**	**SEM**	**N**
10(11)-EpDPE	8.1	0.7	8	8.1	0.5	8	7.4	0.4	8
11(12)-EpETrE	130.6	42.2	8	154.7	36.1	8	149.8	32.0	8
13(14)-EpDPE	218.5	71.7	8	849.7[b,c]	206.6	8	320.5[c]	101.9	8
14(15)-EpETE	38.2	12.6	7	39.4	7.7	8	37.8	8.1	8
14(15)-EpETrE	3.9	1.0	6	2.4	0.4	7	2.3	0.7	8
16(17)-EpDPE	13.6	4.9	7	27.7[b]	5.3	8	12.7	2.7	8
17(18)-EpETE	755.7	264.2	7	766.3	144.2	8	618.9	172.3	8
5(6)-EpETrE	6.3	2.1	6	2.5	0.6	8	3.2	0.8	8
7(8)-EpDPE	30.7	11.6	8	75.5[b]	19.7	8	37.6	8.8	8
8(9)-EpETE	66.8	19.9	6	61.1	16.1	8	63.1	14.4	8
8(9)-EpETrE	2.0	0.6	6	1.5	0.4	7	1.1	0.3	8
9(10)-EpOME	39.3	12.6	7	90.8[b]	21.3	8	42.8	11.2	8
11,12-DiHETrE	151.2	44.3	8	635.4[b,c]	151.2	8	141.7[c]	29.9	8
11(12)-EpETE	2.1	0.2	8	2.9	0.4	8	1.4	0.2	8
12,13-DiHOME	5.2	1.7	8	4.0	1.0	8	3.2	0.4	8
14,15-DiHETE	299.6	92.7	8	542.0	98.7	8	607.2[a]	42.9	8
14,15-DiHETrE	1.3	0.1	8	1.0	0.2	8	0.8	0.1	8
17,18-DiHETE	23.7	3.4	8	30.7	2.5	8	19.5	3.0	8
19(20)-EpDPE	8.6	1.1	8	4.6	0.7	8	4.4	0.6	8
5,15-DiHETE	57.8	15.7	8	80.2	13.4	8	36.8	4.3	8

5,6-DiHETE	543.7	26.4	8	517.5	24.9	7	351.0	41.9	8
5,6-DiHETrE	0.2	0.0	8	0.2	0.0	8	0.1	0.0	8
8,9-DiHETrE	0.2	0.0	8	0.2	0.1	8	0.3	0.1	8
6-keto-PGF1a	170.4	34.9	8	642.7[b]	227.8	8	875.9[a,b]	139.7	8
13-HODE	31.4	4.8	8	82.3	48.0	8	20.6	3.6	8
17-HDoHE	196.5	29.1	8	1074.8[b,c]	564.9	8	167.8[c]	27.7	8
9-HOTrE	114.3	22.6	8	99.0	33.2	8	61.4	7.9	7
9-HODE	19.1	3.7	8	55.1	27.5	8	21.7	4.2	8
20-COOH-LTB4	1.4	0.3	8	7.6[b,c]	4.4	8	1.3[c]	0.2	8
9,10,13-TriHOME	10.6	0.9	8	25.8	10.2	8	9.5	1.0	8
9,12,13-TriHOME	1.2	0.2	8	3.8[b]	1.4	8	1.8	0.3	8
PGB2	15.9	2.9	8	47.8[b]	13.1	8	26.8	3.5	8
20-HETE	61.7	19.1	8	135.4[b]	39.2	8	54.6	16.7	8
9-oxo-ODE	5.0	0.7	7	5.2	0.8	8	4.5	0.5	7
11-HETE	2.2	0.6	8	7.7[b,c]	3.5	8	1.2[c]	0.3	8
12-HEPE	17.1	4.4	7	59.9[c]	25.6	8	10.6[c]	1.7	8
12-HETE	152.2	52.0	8	119.4	74.7	8	31.6[a]	10.5	8
12-oxo-ETE	39.6	9.9	8	132.8[c]	85.3	8	9.2[a,c]	2.5	8
15-oxo-ETE	2.6	0.7	7	5.9[c]	2.5	8	1.7[c]	0.4	7
5-HEPE	5.8	1.9	7	11.8	5.1	8	7.5	1.5	8
5-oxo-ETE	7.6	2.1	8	16.2	5.0	8	7.2	1.2	8

Supplemental Table S2. **List of plasma oxylipins [nM].** Data are represented as mean ± standard error (SEM) and number of samples (N). EpOME: epoxy-octadecenoic acid; DiHOME: dihydroxy-octadecenoic acid; TriHOME: trihydroxyoctadecenoic acid; HOTrE: hydroxy-octadecatrienoic acid; HODE: hydroxy-

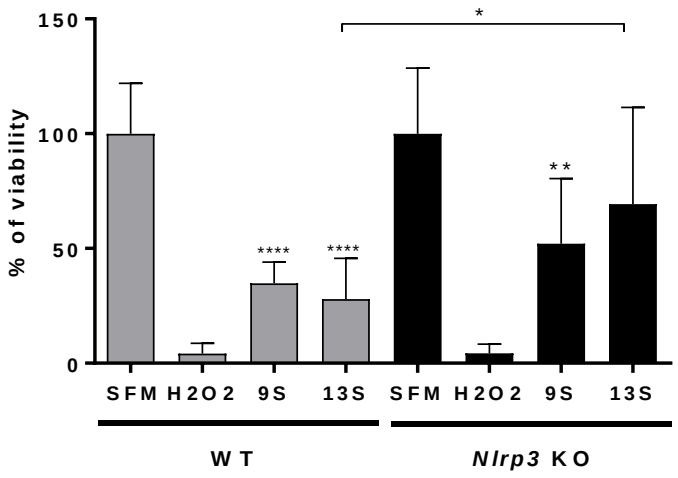
octadecadienoic acid; oxo-ODE: oxo-octadecadienoic acid; HDoHE: hydroxy Docosahexaenoic Acid; PGB: prostaglandin; LTB: Leukotriene; ETE: eicosatetraenoic acid; HETE: hydroxyeicosatetraenoic acid HEPE: hydroxyicosa-pentaenoic acid. Significances were calculated by one-way ANOVA and Sidak post-hoc test of log-transformed data. [a]OXLAMs vs. low LA, [b]high LA vs. low LA, [c]high LA vs. OXLAMs. $p<0.05$ was considered significant. Data sets with more than 30% missing values were not included in the analysis.

Supplemental Figure S1. Effect of high LA and OXLAMs on NADPH oxidase, p38 and apoptosis.



Supplemental Figure S1. (A) mRNA expression of *Nox4* in mouse liver tissue. Gene expression was normalized on housekeeping genes (*Hprt* and *B2M*) and depicted as fold over control. Low LA group was set at 1. (**B)** Serum ALT levels [U/L]. Immunoblot analysis of (**C**) P-p38 and total p38; (**D**) Bax protein, Bid and cleaved Bid (13kDa+15kDa) protein in liver protein lysate. GAPDH and β-Actin were used as loading controls and densitometric analysis was performed on background-subtracted blots and normalized to loading control (GAPDH, β-Actin). The low LA group was set at 1.

Supplemental Figure S2. Primary Hepatocytes from WT and Nlrp3 KO stimulated with OXLAMs.



Supplemental Figure S2. Cell viability assay of primary hepatocytes isolated from WT and global *Nlrp3* KO mice stimulated with OXLAMs. H_2O_2 (0.1%) was used as positive cytotoxic control. OXLAMs (9(S)-and 13(S)-HODE [50uM]) were stimulated in serum-free media (SFM) for 48h. Data were normalized on cells in SFM. Differences between the groups were calculated by one-way ANOVA and Bonferroni selected post-hoc test. Level of significance: $p<0.05$.