

Skoug et al. – Supplementary information

**Table S1.** RT-PCR primers and respective efficiency.

Protein	Mouse gene	Forward primer 5'→3'	Reverse primer 5'→3'	Primer efficiency (%)
ABDH12	<i>Abdh12</i>	CGCTGGGCAGACGAAAGAG	GGAATGGCAATGTAGAACCCC	101
ABDH6	<i>Abdh6</i>	CAATCCTGGCATTGTGCGT	ATGGTGTGCGTAGCGAACTT	104
PNPLA2 (ATGL)	<i>Pnpla2</i>	TCCCACCTTAGCTCCAAGGAT	AGCTTCCTCTGCATCCTCTTC	99
ACACA	<i>Acaca</i>	TACTGCCATCCCATGTGC	GCTTCCAGGAGCAGTCGT	98
CPT1A	<i>Cpt1a</i>	CCAAAACAGTATCCCAATCATCTG	AAGAGACCCCGTAGCCATCA	100
COX1	<i>Cox1</i>	GTGCTGGGGCAGTGCTGGAG	TGGGGCCTGAGTAGCCCGTG	102
COX2	<i>Cox2</i>	CCACTTCAAGGGAGTCT	AGTCATCTGCTACGGGAGGA	105
DAGL $\alpha$	<i>Dagla</i>	GTCCTGCCAGCTTATCTTCCTC	CGTGTGGGTTATAGACCAAGC	99
FASN	<i>Fasn</i>	TTCCAAGACGAAAATGATGC	AATTGTGGGATCAGGAGAGC	106
FAAH	<i>Faah</i>	GCTGTGCTCTTTACCTACCTG	GAAGCATTCTTGAGGCTCAC	99
SLC2A1 (GLUT1)	<i>Slc2a1</i>	CTTCATTGTGGGCATGTGCTTC	AGGTTCCGGCCTTTGGTCTCAG	101
SLC2A3 (GLUT3)	<i>Slc2a3</i>	ATGGGGACAACGAAGGTGAC	GTCTCAGGTGCATTGATGACTC	96
SLC2A4 (GLUT4)	<i>Slc2a4</i>	ACTCTTGCCACACAGGCTCT	AATGGAGACTGATGCGCTCT	105
GLUL	<i>Glul</i>	GCTGCAAGACCCGTACCCT	TTCCACTCAGGTAACTCTCCACA	104
GPM	<i>Pygm</i>	CTTAGCCGGAGTGGAAAATGT	GTAATCTCTCGGAGTAGCCACA	98
GPB	<i>Pygb</i>	CTTAGCCGGAGTGGAAAATGT	GTAATCTCTCGGAGTAGCCACA	97
HK1	<i>Hk1</i>	TATCGGTCCAGCACGTATGC	AGAACCGTCTACGCCAACTG	100
IL-10	<i>Il10</i>	ATGGTGTCTTTCAATTGCTC	AGGATCTCCCTGGTTTCTCTT	100
IL-6	<i>Il6</i>	TCTGAAGGACTCTGGCTTTG	GATGGATGCTACCAAAGTGA	101
IL-1 $\beta$	<i>Il1B</i>	GAAGAGCCCATCCTCTGTGA	TTCATCTCGGAGCCTGTAGTG	103
LPL	<i>Lpl</i>	AGGTGGACATCGGAGAACTG	TTTGTCCAGTGTCAGCCAGA	99
MAGL	<i>Magl</i>	GTGCCTACCTGCTCATGGAAT	GAGGACGGAGTTGGTCACTTC	97
PGC1 $\alpha$ -1 *	<i>Pparg1a</i>	GGACATGTGCAGCCAAGACTCT	CACTTCAATCCACCCAGAAAGCT	100
PGC1 $\alpha$ -4 *	<i>Pparg1a</i>	TCACACCAAACCCACAGAAA	CTGGAAGATATGGCACAT	97
PGC1 $\alpha$	<i>Pparg1a</i>	TGATGTGAATGACTTGGATACAGACA	GCTCATTGTTGACTGGTTGGATATG	99
NF- $\kappa$ B	<i>Nfkb1</i>	CGGAGGACGGAGACTCGTT	CCATGGTCAGCGGCTTCT	101
PPAR $\gamma$	<i>Pparg</i>	GGTCAGCTCTTGTGAATGGAA	ATCAGCTCTGTGGACCTCTCC	98
TNF- $\alpha$	<i>Tnf</i>	TTGACCTCAGCGCTGAGTTG	CCTGTAGCCCACGTCGTAGC	104

\*result from alternative splicing of *Pparg1a*

**Table S2.** Oxylipins detected in the lipidomics analysis, their retention times and multiple reaction monitoring transitions, mean concentrations (pg/mg of tissue) in cortex and hippocampus, and concentration change (%) for HSL<sup>-/-</sup> versus HSL<sup>+/+</sup> mice.

Name	Abbreviation	Retention time (min)	Precursor > Product	Mean concentration in hippocampus			Mean concentration in cortex		
				HSL <sup>+/+</sup>	HSL <sup>-/-</sup>	% change	HSL <sup>+/+</sup>	HSL <sup>-/-</sup>	% change
6-keto-prostaglandin F1 $\alpha$	6-keto-PGF1 $\alpha$	6	369 > 163	1.69	1.24	-27%	1.35	1.45	8%
Thromboxane B2	TxB2	7.8	369.23 > 169.1	14.78	15.04	2%	38.86	40.48	4%
9,10,13-Trihydroxy-11-octadecenoic acid	9,10,13-TriHOME	8.2	329.23 > 171	6.07	5.73	-6%	3.83	4.22	10%
9,12,13-Trihydroxy-10-octadecenoic acid	9,12,13-TriHOME	8.4	329.23 > 211.1	6.21	5.83	-6%	3.96	4.29	8%
Prostaglandin E2	PGE2	8.4	351.21 > 315.1	23.62	19.85	-16%	29.45	30.55	4%
Prostaglandin F2 $\alpha$	PGF2 $\alpha$	8.6	353.23 > 193.3	32.76	34.56	5%	76.67	93.01	21%
8-iso Prostaglandin E2	8-iso-PGE2	9.05	351.21 > 271.1	74.73	64.29	-14%	156.32	141.66	-9%
Prostaglandin D2	PGD2	9.35	351.21 > 315.2	77.17	65.02	-16%	157.21	138.78	-12%
5(s)6(R) lipoxin A4	5(s)6(R)-LXA4	10	351 > 115	0.21	0.21	1%	0.14	0.15	9%
Trans-Leukotriene B4	trans-LTB4	12.4	335.22 > 195.1	0.14	0.15	6%	0.16	0.14	-10%
Leukotriene B4	LTB4	13.06	335.22 > 195.1	0.21	0.23	11%	0.13	0.14	9%
12,13-Dihydroxyoctadec-9(Z)-enoic acid	12,13-DiHOME	13.6	313.24 > 183.2	1.58	1.42	-10%	1.50	1.41	-6%
9,10-Dihydroxyoctadec-12(Z)-enoic acid	9,10-DiHOME	13.89	313.24 > 201	0.76	0.70	-8%	0.66	0.64	-2%
11,12-dihydroxyeicosatrienoic acid	11,12-DiHETrE	14.6	337.24 > 167.1	0.25	0.23	-9%	0.28	0.28	-1%
14,15-Dihydroxyeicosatrienoic acid	14,15-DiHETrE	14.6	337.24 > 207	0.57	0.51	-10%	0.65	0.64	-2%
8,9-Dihydroxyeicosatrienoic acid	8,9-DiHETrE	15.6	337.24 > 127.2	0.34	0.32	-5%	0.33	0.32	-4%
20-Hydroxyarachidonic acid	20-HETE	16	319.23 > 289.2	0.75	0.62	-18%	1.90	1.51	-20%
5,6-dihydroxy-8Z,11Z,14Z-icosatrienoic acid	5,6-DiHETrE	16.21	337.24 > 71	0.94	0.82	-13%	0.86	0.87	1%
(12S)-12-hydroxyeicosapentaenoic acid	12(S)-HEPE	16.3	317.21 > 179.1	0.25	0.22	-12%	0.41	0.60	48%
13-hydroxy-cis-9,trans-11-octadecadienoic acid	13-HODE	17	295.23 > 195.1	37.36	23.01	-38%	18.37	8.94	-51%
13-Oxo-9Z,11E-octadecadienoic acid	13-oxo-ODE	17	293.21 > 113.1	13.09	5.85	-55%	12.51	5.68	-55%
9(S)-hydroxyoctadecadienoic acid	9(S)-HODE	17	295.23 > 171.2	15.24	8.49	-44%	14.56	8.36	-43%
17-hydroxydocosahexaenoic acid	17-HDOHE	17.48	343.23 > 281.2	24.14	15.42	-36%	20.86	10.72	-49%
15-ketoeicosatetraenoic acid	15-oxo-ETE	17.6	317.21 > 113.2	435.76	296.70	-32%	261.06	187.52	-28%
15-hydroxy-5Z,8Z,11Z,13E-icosatetraenoic acid	15-HETE	17.7	319.23 > 219	15.50	14.69	-5%	18.27	17.93	-2%
11-hydroxy-5Z,8Z,11E,14Z-icosatetraenoic acid	(+)-11-HETE	17.9	319.23 > 167.2	12.77	10.36	-19%	21.26	19.59	-8%

12-Hydroxy-5,8,10,14-eicosatetraenoic acid	12-HETE	18	319.23 > 179.1	90.67	75.08	-17%	72.84	86.28	18%
15(S)-Hydroxyeicosatrienoic acid	15(S)-HETrE	18.13	321.24 > 303.3	1.92	1.12	-42%	2.20	1.42	-35%
8(S)-hydroxyeicosatetraenoic acid	8(S)-HETE	18.27	319.23 > 155	14.94	14.72	-1%	7.62	8.85	16%
5-Hydroxyeicosatetraenoic acid	5-HETE	18.3	319.23 > 115.1	47.29	47.51	0%	28.96	33.31	15%
9-hydroxy-5Z,7E,11Z,14Z-eicosatetraenoic acid	(+/-)9-HETE	18.5	319.23 > 167.2	418.82	279.08	-33%	258.39	180.12	-30%
12-oxo-5Z,8Z,10E,14Z-eicosatetraenoic acid	12-OxoETE	18.5	317.21 > 273.1	15.07	16.01	6%	8.20	11.09	35%
9,10-Epoxyoctadecenoic acid	9,10-EpOME	18.9	295.23 > 171.2	0.07	0.07	-9%	0.07	0.07	5%
14,15-epoxyeicosatrienoic acid	14,15-EpETrE	19.06	319.23 > 219	21.73	21.18	-3%	8.43	11.32	34%
5-ketoeicosatetraenoic acid	5-oxo-ETE	19.1	317.21 > 203.2	19.99	21.35	7%	14.50	16.11	11%
11,12-epoxyeicosatrienoic acid	11,12-EpETrE	19.4	319.23 > 167.1	10.34	8.62	-17%	3.48	4.19	20%
5,6-epoxyeicosatrienoic acid	5,6-EpETrE	19.4	319.23 > 191.1	9.59	9.11	-5%	4.36	5.48	26%
8,9-epoxyeicosatrienoic acid	8,9-EpETrE	19.4	319.23 > 69.2	679.39	541.97	-20%	245.07	248.88	2%

**Table S3.** Endocannabinoids detected in the lipidomics analysis, their retention times and multiple reaction monitoring transitions, mean concentrations (pg/mg of tissue) in cortex and hippocampus, and concentration change (%) for HSL<sup>-/-</sup> versus HSL<sup>+/+</sup> mice.

Name	Abbreviation	Retention time (min)	Precursor > Product	Mean concentration in hippocampus			Mean concentration in cortex		
				HSL <sup>+/+</sup>	HSL <sup>-/-</sup>	% change	HSL <sup>+/+</sup>	HSL <sup>-/-</sup>	% change
Prostaglandin F2 $\alpha$ ethanolamide	PGF2 $\alpha$ EA	3.19	380 > 62	0.15	0.14	-4%	0.09	0.09	2%
Prostaglandin E2 ethanolamide	PGE2 EA	3.24	378 > 62	1.15	1.07	-7%	0.66	0.50	-24%
Eicosapentaenoylethanolamide	EPEA	5.66	346 > 62	0.02	0.01	-22%	0.02	0.02	0%
Palmitoleoylethanolamide	POEA	6.27	298 > 62	1.03	1.21	18%	4.03	3.43	-15%
Docosahexaenoylethanolamide	DHEA	6.31	372 > 62	2.62	2.69	3%	10.35	7.66	-26%
Arachidonylethanolamide (anandamide)	AEA	6.58	348 > 62	3.46	3.12	-10%	9.26	8.67	-6%
N-Arachidonoylglycine	NAGly	6.66	362 > 287	11.76	9.12	-22%	12.42	11.94	-4%
Linoleoylethanolamide	LEA	6.72	324 > 62	1.81	1.70	-6%	8.37	7.09	-15%
2-Arachidonoylglycerol	2-AG	7.3	379 > 287	2912.07	2508.09	-14%	2097.79	2191.85	4%
2-Linoleoylglycerol	2-LG	7.63	355 > 263	96.67	84.02	-13%	119.71	95.20	-20%
Docosatetraenoylethanolamide	DEA	8.21	376 > 62	0.28	0.30	7%	0.91	0.92	1%
N-Oleoylethanolamine	OEA	8.52	326 > 62	10.51	9.64	-8%	21.00	22.92	9%
Stearoylethanolamide	SEA	11.85	328 > 62	18.25	16.96	-7%	10.97	11.34	3%

**Figure S1.** Tukey plots showing relative expression of genes coding for metabolism proteins or cytokines in the hippocampus and cortex of HSL<sup>-/-</sup> mice relative to wild-type littermates. \*P<0.05, \*\*P<0.01 in Student t-tests.

