Supplemental Figure Legends

Figure S1. Selectivity of the FAAH antibody. (*A*) Representative western blot of FAAH in skin and liver extracts from wild-type and *Faah*$^{-/-}$ mice. Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was used as loading control. (*B*) Representative single-labeling immunofluorescence for FAAH (green) in skin sections of wild-type and *Faah*$^{-/-}$ mice; cell nuclei are stained with DAPI (blue). Scale bar, 20 µm.

Figure S2. Double immunofluorescence for FAAH and fatty acid-binding protein-4 (FABP4). Nuclei are stained with DAPI (blue, *A* and *A1*); representative immunofluorescence images for FAAH (green, *B* and *B1*) and FABP4 (red, *C* and *C1*); merged channels images are shown in *D* and *D1*. Scale bars, 100 µm in *D* and 20 µm in *D1*.

Figure S3. Representative western blot of FAAH in epidermis and dermis of wild-type mice. Skin layer separation was performed mechanically, after tissue digestion with dispase. GAPDH was used as loading control.

Figure S4. Immunofluorescence for vimentin in mouse skin. Representative images of wounded skin of *Faah*$^{-/-}$ mice (*A* and *A1*) immunostained (red) for vimentin; cell nuclei are stained with DAPI (blue *A* and *A1*). Scale bars, 100 µm in *A* and 50 µm in *A1*.

Figure S5. Immunofluorescence for cytokeratin 5 (K5), cytokeratin 10 (K10) and filaggrin in mouse skin. Representative images of wounded skin of wild-type (*A-C* and *A1-C1*) and *Faah*$^{-/-}$ mice (KO, *D-F* and *D1-F1*) immunostained (red) for K5 (*A*, *A1* and *D*, *D1*), K10 (*B*, *B1* and *E*, *E1*) and filaggrin (*C*, *C1* and *F*, *F1*); cell nuclei are stained with DAPI (blue *A-F* and *A1-F1*). Scale bars, 100 µm in *A* and 50 µm in *A1*.

Figure S6. Score Plot, positive ion mode, for the Principal Component Analysis on the data set reported in Fig. 4. Wild-type mice (black dots) and *Faah*$^{-/-}$ mice (red dots) are differentially clustered, indicating significant differences in their skin lipidome.

Figure S7. Tandem MS data (negative ion mode) for (a) NAT(24:0) and (b) NAT(20:0) in skin of *Faah*$^{-/-}$ mice, acquired at 40eV collision energy. For each compound the MS/MS spectrum of authentic standard (upper trace) is compared to the MS/MS spectrum of skin-derived compound (lower trace). The *m/z* = 50-200 region is magnified ten folds to improve visibility of diagnostic fragment ions. For NAT(24:0), the MS/MS spectrum stored in the METLIN database (40eV) is also reported (*A*, inset).

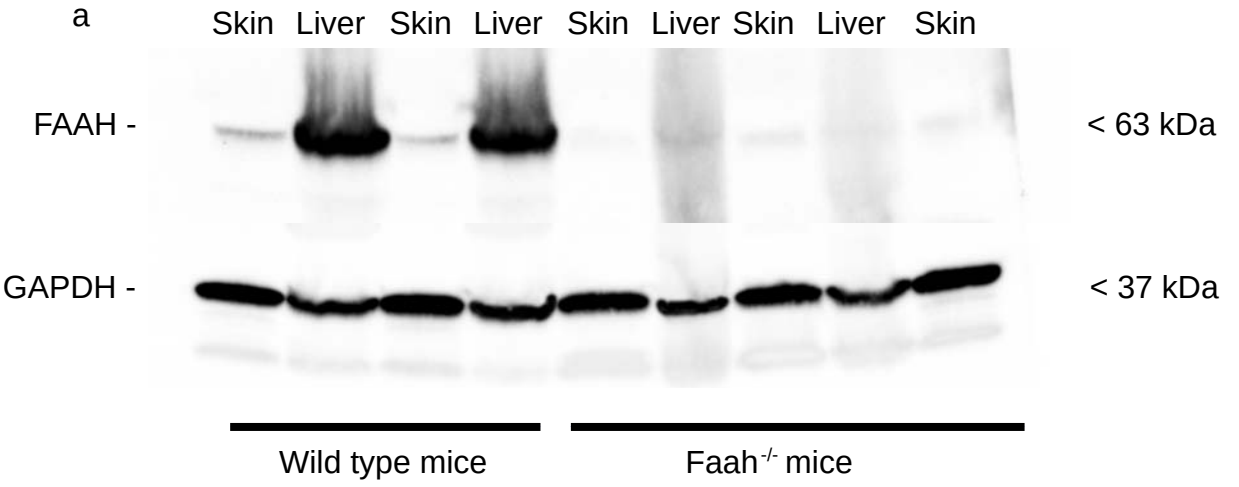
Figure S8. Hematoxylin-eosin staining of representative skin sections from wild-type mice treated with vehicle (*A* and *A1*) or NAT(20:0) (*B* and *B1*). Scale bars, 500 μm in *A*, and *B* and 50 μm in *A1* and *B1*.

Figure S9. Effects of OEA on excisional skin wound healing. Time-course (days) of wound healing in mice treated with vehicle (open bars) or various doses (%) of OEA. *P<0.05, **P<0.01 and ***P<0.001 compared to vehicle or wild-type mice, two-way ANOVA; n=9.

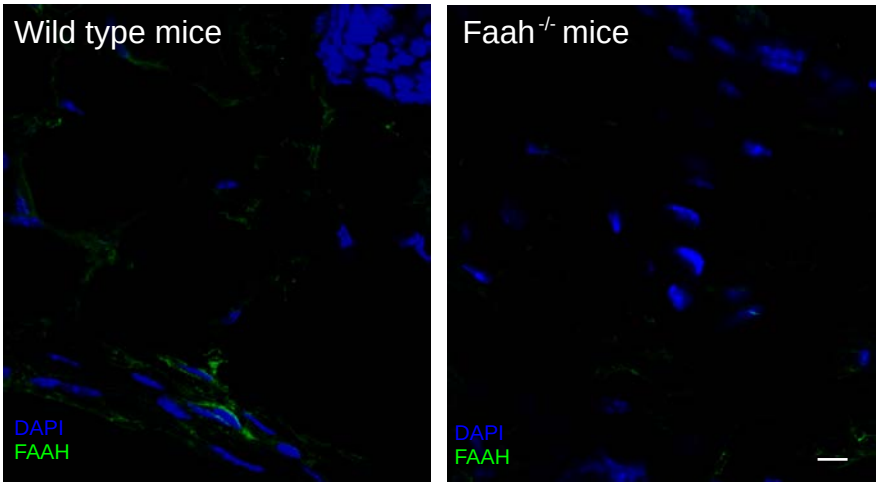
Figure S10. Effects of synthetic (*A*) NAT(24:0) and (*B*) NAT(20:0) (each at 0.001-3 μM) on intracellular calcium levels in Chinese hamster ovary cells expressing human TRPV1. Data are shown as percentage of response elicited by the reference agonist, capsaicin (1 μM).

Supplemental Figure 1

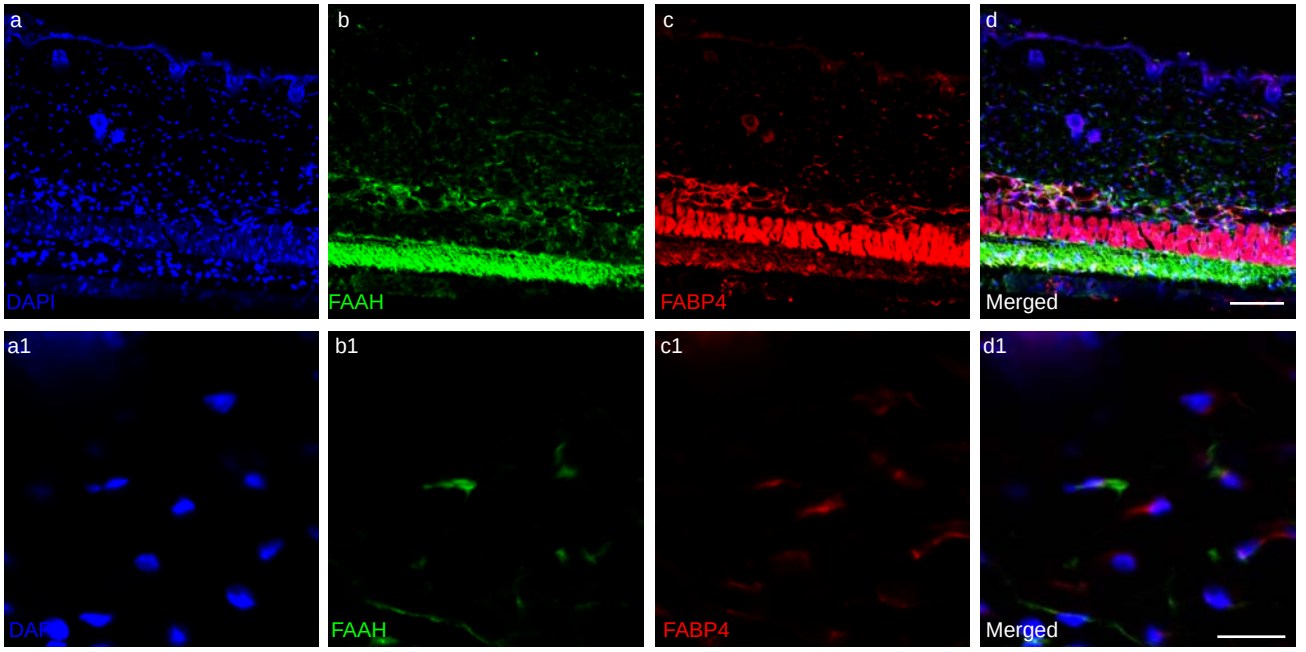
a



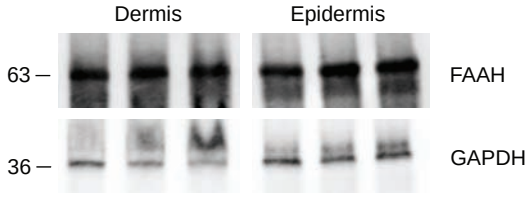
b



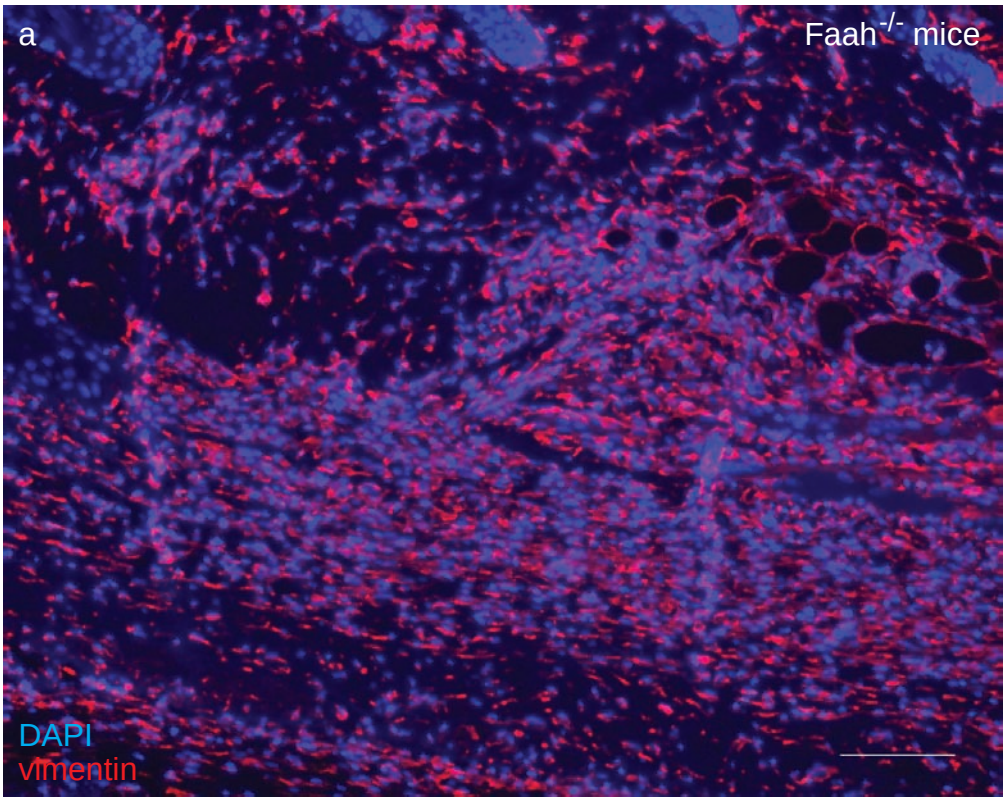
Supplemental Figure 2

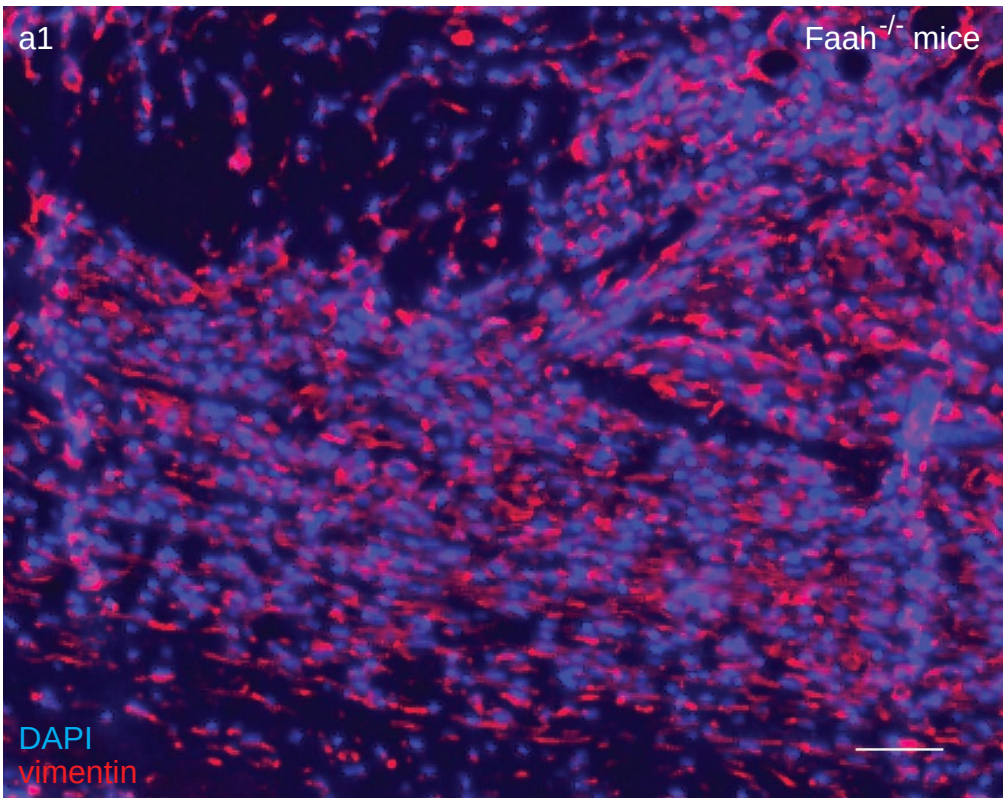


Supplemental Figure 3

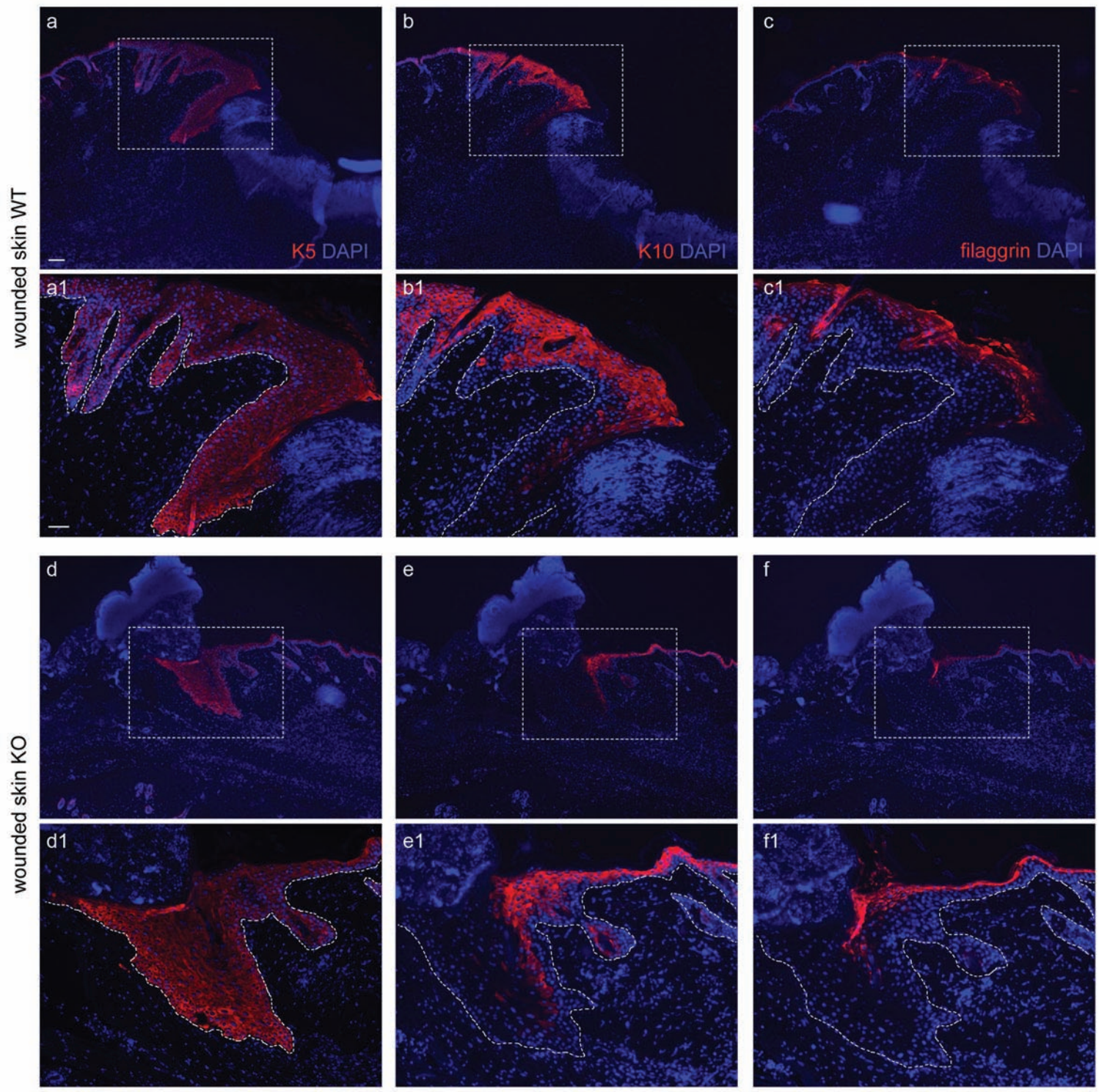


Supplemental Figure 4

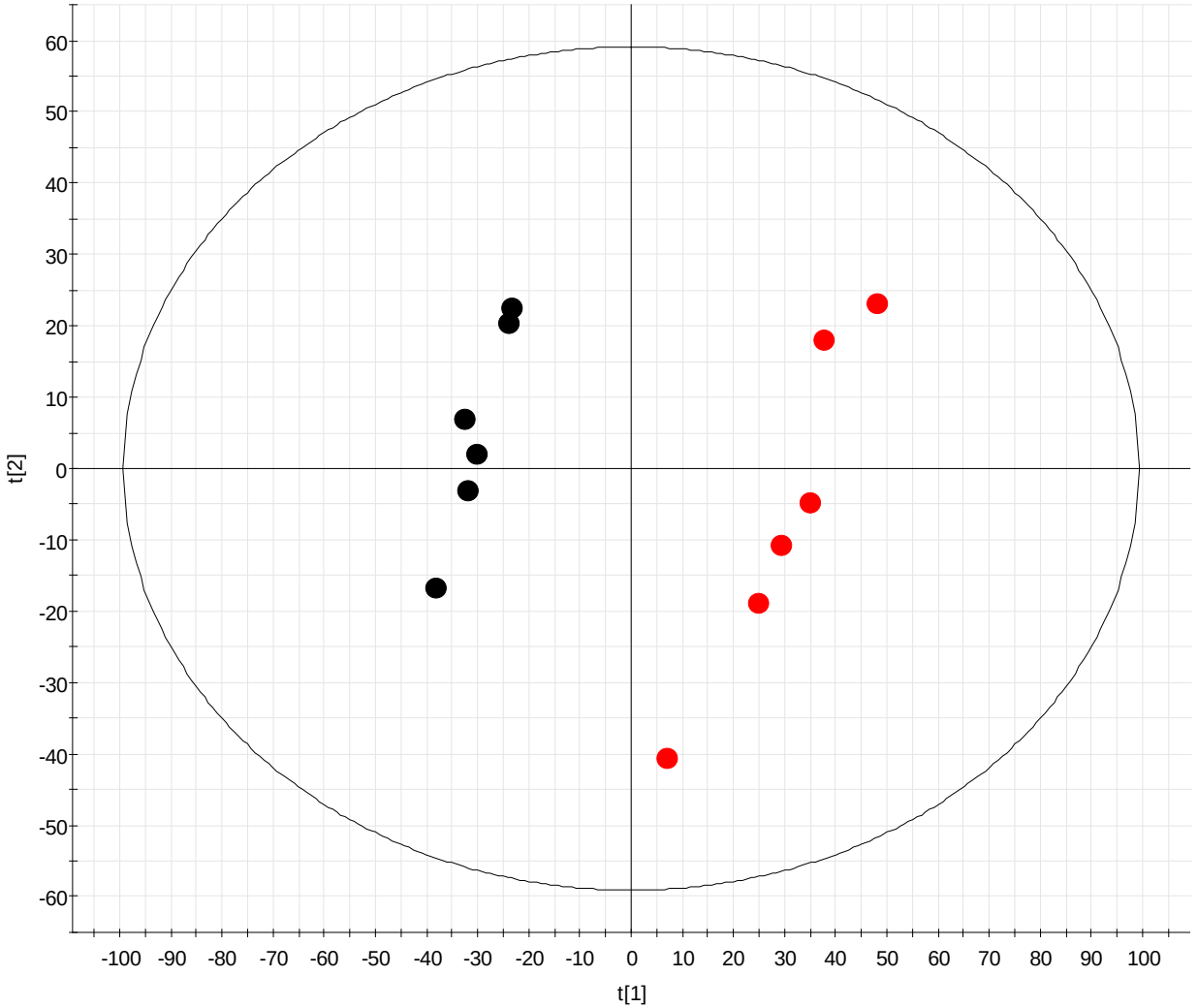


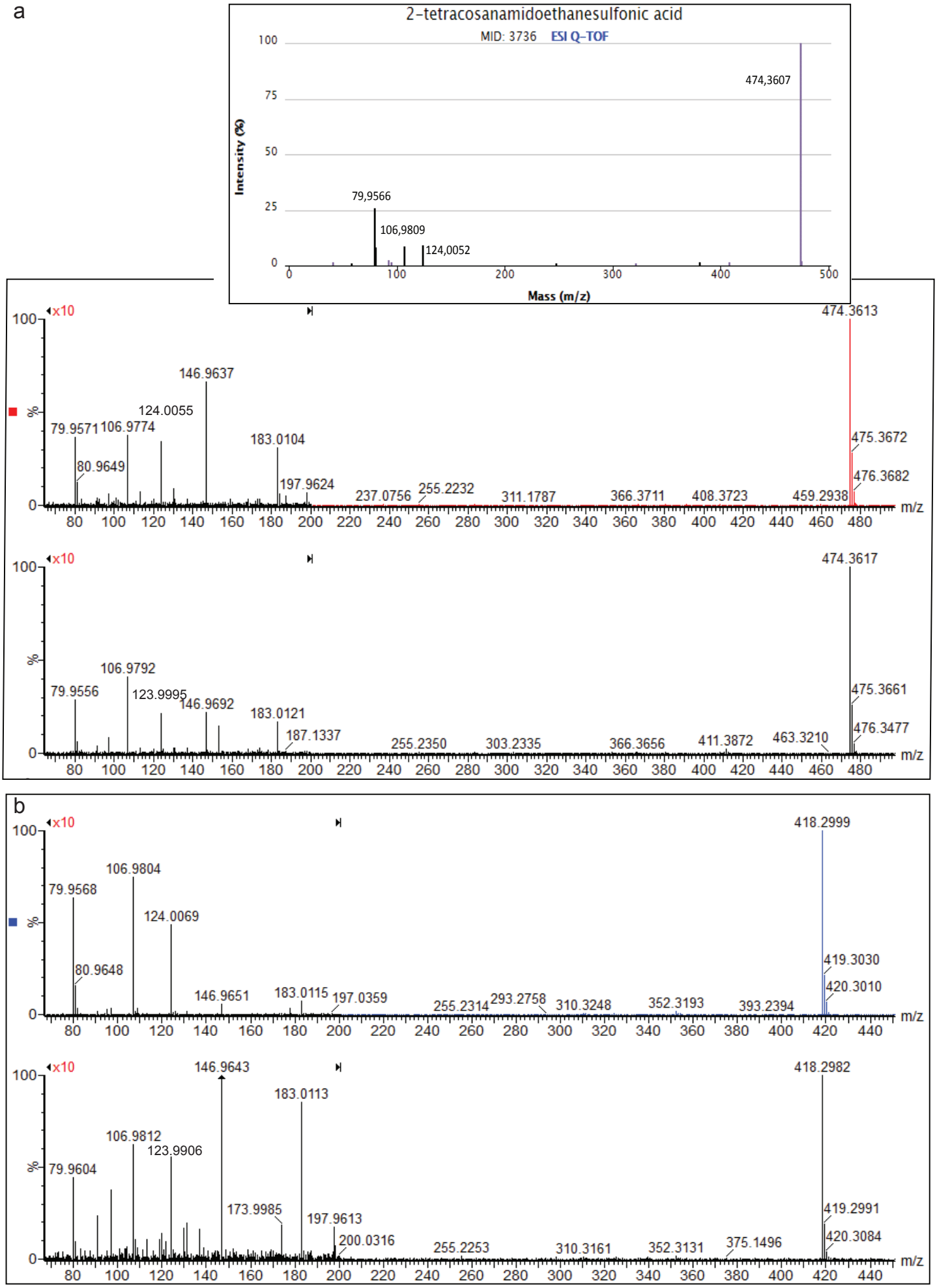


Supplemental Figure 5



Supplemental Figure 6




a
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Intensity (%)
Mass (m/z)
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124,0052
x10
474.3613
146.9637
124.0055
79.9571
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m/z
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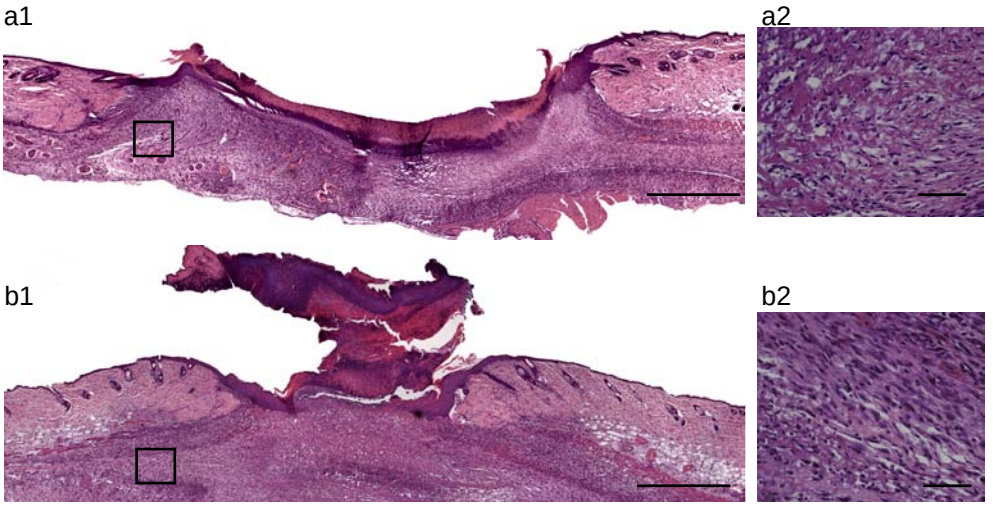
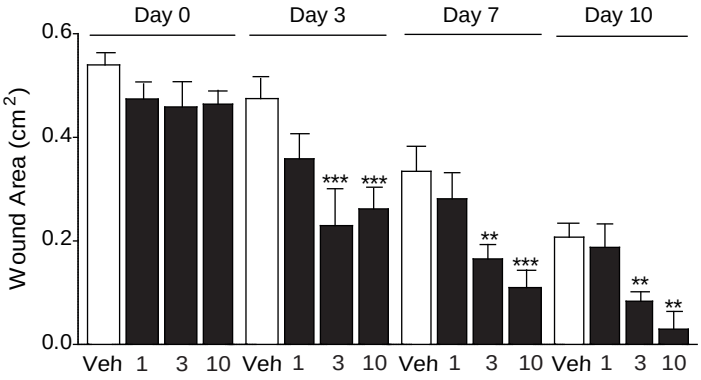
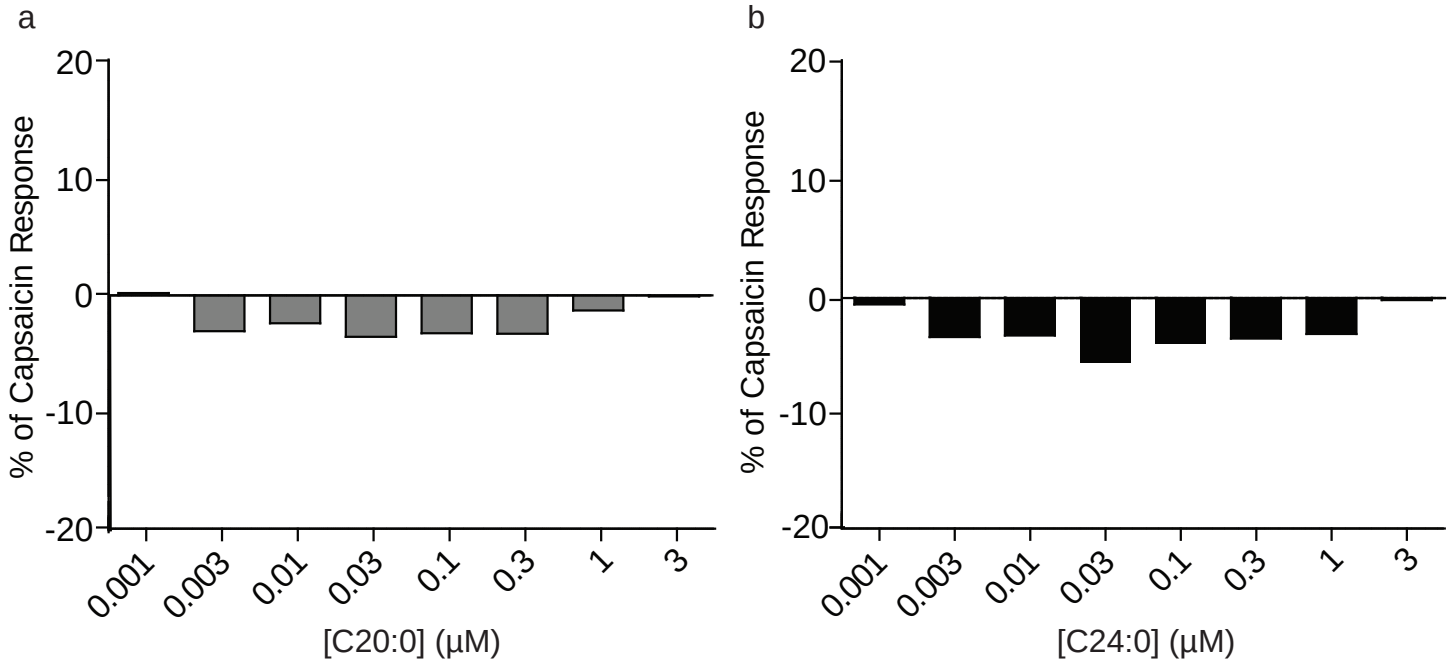
Supplemental Figure 8



Supplemental Figure 9



Supplemental Figure 10



Supplementary Table 1: Untargeted lipidomics analysis of skin in wild-type (WT) and *Faah*$^{-/-}$ mice, negative ion mode. Columns marked WT and *Faah*$^{-/-}$ show signal intensities for all analytes detected in the two sets of samples.

Abbreviations:

FAE	Fatty Acyl Ethanolamide
FA	Fatty Acid
PA	Phosphatidic Acid
PE	Phosphatidylcholine
PC	Phosphatidylethanolamine
NAG	N-Acyl Glycine
NAT	N-Acyl Taurine
Cer	Ceramide
MG	Monoacylglycerol
DG	Diacylglycerol
WE	Wax Ester

Lipid Class	Type	Tentative Identificaiton	Adduct Type	ppm	RT	*m/z*	WT	*Faah* -/-	P-value	Percent Change	Regulation in *Faah*$^{-/-}$
Fatty Acyl	N-Acyl Taurine	25:0 NAT	[M-H]-	1	8,25	488.3770	**0,004**	**0,088**	1,3E-06	2237%	UP
Fatty Acyl	N-Acyl Taurine	24:0 NAT	[M-H]-	2	7,79	474.3611	**0,083**	**1,546**	5,6E-07	1757%	UP
Fatty Acyl	N-Acyl Taurine	26:0 NAT	[M-H]-	4	8,67	502.3915	**0,006**	**0,079**	2,5E-05	1173%	UP
Fatty Acyl	N-Acyl Taurine	24:1 NAT	[M-H]-	0	6,75	472.3462	**0,005**	**0,057**	2,6E-06	1172%	UP
Fatty Acyl	N-Acyl Taurine	23:0 NAT	[M-H]-	3	7,30	460.3448	**0,008**	**0,092**	7,4E-06	1051%	UP
Fatty Acyl	N-Acyl Taurine	22:0 NAT	[M-H]-	1	6,75	446.3302	**0,016**	**0,169**	1,9E-06	964%	UP
Fatty Acyl	N-Acyl Taurine	20:0 NAT	[M-H]-	2	5,49	418.2978	**0,033**	**0,121**	5,2E-05	265%	UP
Fatty Acyl	Fatty Acid	28:1 FA	[M-H]-	4	10,79	421.4032	**0,043**	**0,109**	7,3E-03	155%	UP
Fatty Acyl	Fatty Acid	22:1 FA	[M-H]-	1	8,47	337.3107	**0,319**	**0,746**	5,4E-05	134%	UP
Fatty Acyl	Fatty Acid	21:0 FA	[M-H]-	4	8,81	325.3097	**0,061**	**0,124**	9,7E-07	103%	UP
Fatty Acyl	Fatty Acid	19:0 FA	[M-H]-	3	7,71	297.2788	**0,068**	**0,137**	1,3E-05	102%	UP
Fatty Acyl	Fatty Acid	16:1 FA	[M-H]-	3	4,68	253.2163	**2,968**	**5,847**	7,2E-04	97%	UP
Fatty Acyl	Fatty Acid	16:0 FA	[M-H]-	4	5,77	255.2317	**0,027**	**0,051**	1,1E-03	92%	UP

Fatty Acyl	N-Acyl Glycine	18:0 NAG	[M-H]-	5	12,23	340.2839	**0,079**	**0,142**	2,3E-02	80%	UP
Fatty Acyl	Fatty Acid	26:1 FA	[M-H]-	3	10,13	393.3723	**0,061**	**0,109**	3,4E-04	79%	UP
Fatty Acyl	Fatty Acid	24:1 FA	[M-H]-	2	9,37	365.3415	**0,193**	**0,339**	5,0E-04	75%	UP
Sphingolipid	Ceramide	Cer(t18:0/18:0)	[M-H]-	3	10,62	582.5396	**0,054**	**0,090**	3,3E-04	66%	UP
Fatty Acyl	Wax Ester	WE(16:1/14:0)	[M-H]-	0	11,34	449.4360	**0,114**	**0,188**	2,6E-04	64%	UP
Fatty Acyl	Hydroxy Fatty Acid	18:1(OH) FA	[M-H]-	2	2,95	297.2412	**0,049**	**0,079**	1,2E-05	61%	UP
Fatty Acyl	Fatty Acid	20:2(OH) FA	[M-H2O-H]-	3	5,87	305.2471	**0,128**	**0,203**	4,0E-04	58%	UP
Fatty Acyl	Fatty Acid	22:6 FA	[M-H]-	2	7,62	327.2334	**0,035**	**0,054**	2,7E-04	57%	UP
Fatty Acyl	Fatty Acid	17:0 FA	[M-H]-	2	6,44	269.2479	**0,091**	**0,142**	2,4E-05	56%	UP
Sphingolipid	Ceramide	Cer(d18:1/16:0(OH)	[M+FA-H]-	2	10,06	598.5036	**0,142**	**0,220**	2,1E-02	56%	UP
Sphingolipid	Ceramide	Cer(d18:1/20:0)	[M-H]-	1	11,42	592.5665	**0,231**	**0,350**	6,8E-04	52%	UP
Fatty Acyl	Fatty Acid	20:5 FA	[M-H]-	2	3,91	301.2165	**0,123**	**0,177**	1,4E-03	44%	UP
Fatty Acyl	Hydroxy Fatty Acid	16:0(OH) FA	[M-H]-	1	2,58	271.2274	**0,132**	**0,188**	1,3E-04	42%	UP
Fatty Acyl	Wax Ester	WE(16:1/16:0)	[M-H]-	5	11,83	477.4631	**0,259**	**0,367**	5,0E-03	42%	UP
Fatty Acyl	Dicarboxylic Fatty Acid	30:0 Dicarboxylic FA	[M-H]-	1	9,44	467.4464	**0,269**	**0,379**	1,8E-03	41%	UP
Sphingolipid	Ceramide	Cer(d18:1/16:0)	[M+FA-H]-	1	10,34	582.5096	**0,773**	**1,067**	1,5E-03	38%	UP
Fatty Acyl	Fatty Acid	24:6 FA	[M-H]-	2	5,59	355.2632	**0,033**	**0,045**	1,1E-03	38%	UP
Fatty Acyl	Dicarboxylic Fatty Acid	24:0 Dicarboxylic FA	[M-H]-	3	8,08	397.3304	**0,064**	**0,088**	2,3E-02	36%	UP
Fatty Acyl	Keto Fatty Acid	20:1 (O) FA	[M+FA-H]-	4	9,80	453.3930	**0,040**	**0,055**	3,4E-02	36%	UP
Sphingolipid	Ceramide	Cer(d18:1/16:1)	[M-H]-	4	9,77	534.4866	**0,046**	**0,062**	2,2E-02	35%	UP
Fatty Acyl	Fatty Acid	20:0 FA	[M-H]-	3	8,45	311.2945	**0,104**	**0,138**	3,7E-03	34%	UP
Fatty Acyl	Dicarboxylic Fatty Acid	31:0 Dicarboxylic FA	[M-H]-	2	10,46	481.4232	**0,061**	**0,081**	2,8E-02	33%	UP
Fatty Acyl	Hydroxy Fatty Acid	28:0(OH) FA	[M-H]-	0	8,68	439.4156	**0,036**	**0,047**	1,7E-02	32%	UP
Fatty Acyl	Dicarboxylic Fatty Acid	26:0 Dicarboxylic FA	[M-H]-	2	9,02	425.3669	**0,096**	**0,125**	1,7E-02	31%	UP
Fatty Acyl	Acyl-carnitine	26:0 Carnitine	[M-H]-	2	9,72	538.4828	**1,998**	**2,612**	1,4E-02	31%	UP

Fatty Acyl	Fatty Acid	21:1 FA	[M-H]-	2	7,95	323.2947	**0,121**	**0,083**	3,8E-03	-31%	DOWN
GlyceroPhospho Lipid	Lysophosphatidylcholine	LysoPC(16:0)	[M-H]-	2	4,00	494.3239	**0,062**	**0,039**	9,6E-04	-36%	DOWN
Fatty Acyl	Fatty Acid	24:4 FA	[M-H]-	1	7,09	359.2949	**0,054**	**0,034**	3,2E-05	-38%	DOWN
GlyceroPhospho Lipid	Lysophosphatidylethanolamine	LysoPE(22:4)	[M-H]-	1	2,18	528.3086	**0,108**	**0,064**	2,2E-05	-41%	DOWN
Glycerolipid	Monoacylglycerol	(O-16:0/0:0/0:0) MG	[M-H2O-H]-	4	7,93	297.2781	**0,049**	**0,029**	4,8E-02	-41%	DOWN
Sterol Lipid	Vit d3 Derivative	1a,25-dihydroxy-11-(3-hydroxy-1-propynyl)-9,11-didehydrovitamin D3	[M-H]-	3	6,68	467.3183	**0,036**	**0,021**	4,3E-03	-42%	DOWN
GlyceroPhospho Lipid	Lysophosphatidylcholine	LysoPC(20:4)	[M-H]-	1	2,18	588.3298	**0,055**	**0,030**	4,4E-04	-46%	DOWN
GlyceroPhospho Lipid	Lysophosphatidylcholine	LysoPC(18:0)	[M-H]-	1	4,47	568.3612	**0,037**	**0,016**	5,8E-05	-57%	DOWN
GlyceroPhospho Lipid	Lysophosphatidylethanolamine	LysoPE(20:0)	[M-H]-	0	4,46	508.3407	**0,064**	**0,026**	7,3E-05	-60%	DOWN
Sphingolipid	Ceramide	Cer(d18:0/18:0)	[M-H]-	5	10,38	566.5153	**0,295**	**0,117**	3,4E-04	-60%	DOWN
Sterol Lipid	Vitamin D3 Derivative	1a-hydroxy-18-[m-(1-hydroxy-1-ethylpropyl)-benzyloxy]-23,24,25,26,27-pentanorcholecalciferol	[M-H2O-H]-	3	8,23	503.3510	**0,047**	**0,017**	2,5E-05	-63%	DOWN
Fatty Acyl	Hydroxy Fatty Acid	19:1 (OH) FA	[M-H]-	0	3,55	311.2590	**0,102**	**0,037**	1,0E-05	-64%	DOWN
Glycerolipid	Monoacylglycerol	24:0 MG	[M+FA-H]-	0	9,59	487.4005	**0,044**	**0,015**	3,6E-02	-66%	DOWN
GlyceroPhospho Lipid	Lysophosphatidic Acid	LysoPA(16:0)	[M-H]-	3	3,25	391.2242	**0,048**	**0,016**	6,8E-05	-67%	DOWN
GlyceroPhospho Lipid	Lysophosphatidic Acid	LysoPA(18:0)	[M-H]-	2	4,75	419.2545	**0,038**	**0,011**	6,8E-04	-72%	DOWN
Fatty Acyl	Fatty Acid	19:1 FA	[M-H]-	4	6,78	295.2630	**0,220**	**0,051**	5,4E-03	-77%	DOWN
GlyceroPhospho Lipid	Lysophosphatidylcholine	LysoPC(18:1)	[M-H]-	4	4,18	520.3387	**0,049**	**0,008**	3,1E-07	-84%	DOWN

Supplementary Table 2: Untargeted lipidomics analysis of skin in wild-type (WT) and *Faah*$^{-/-}$ mice, positive ion mode. Columns marked WT and *Faah*$^{-/-}$ show signal intensities for all analytes detected in the two sets of samples.

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NAT	N-Acyl Taurine
Cer	Ceramide
MG	Monoacylglycerol
DG	Diacylglycerol
WE	Wax Ester
GABA	Gamma Aminobutyric Acid

Lipid Class	Type	Tentative ID	Adduct Type	ppm	RT	*m/z*	WT	*Faah* -/-	P-value	Percent Change	Regulation in *Faah*-/-
Fatty Acyl	N-Acyl Taurine	26:0 NAT	[M+H]+	2	8,70	504.4069	**0,00**	**0,23**	1,8E-02	22948%	UP
Fatty Acyl	N-Acyl Taurine	24:0 NAT	[M+H]+	1	7,85	476.3776	**0,29**	**5,44**	7,5E-06	1761%	UP
Fatty Acyl	N-Acyl Taurine	25:0 NAT	[M+H]+	2	8,30	490.3913	**0,02**	**0,27**	5,9E-06	1422%	UP
Fatty Acyl	N-Acyl Taurine	23:0 NAT	[M+H]+	2	7,36	462.3601	**0,02**	**0,25**	1,9E-05	1192%	UP
Fatty Acyl	N-Acyl Taurine	22:0 NAT	[M+H]+	1	6,80	448.3447	**0,04**	**0,32**	6,4E-05	643%	UP
Fatty Acyl	Oxygenated hydrocarbon	32:0 (O)	[M+NH4]+	2	12,16	482.5308	**0,05**	**0,19**	4,9E-03	288%	UP
Glycerolipid	Diacylglycerol	(32:3) DG	[M+H]+	4	10,63	397.3321	**0,09**	**0,16**	3,5E-02	88%	UP
Glycerolipid	Diacylglycerol	(32:1) DG	[M-H2O+H]+	3	10,80	567.4997	**0,45**	**0,81**	4,5E-03	81%	UP
Sphingolipid	Ceramide	Cer(d18:1/20:2)	[M+H]+	1	10,98	590.5516	**2,95**	**5,18**	1,1E-02	76%	UP
Fatty Acyl	Wax ester	Retinyl linoleate	[M+H]+	3	13,18	549.4848	**0,12**	**0,20**	3,5E-03	63%	UP
Fatty Acyl	Wax ester	WE(18:1/18:1)	[M+H]+	3	12,81	533.5312	**0,11**	**0,17**	7,8E-04	60%	UP
Fatty Acyl	N-Acyl amines	N-palmitoyl GABA	[M+H]+	5	6,60	342.3362	**0,15**	**0,24**	1,9E-03	59%	UP
Fatty Acyl	Acyl-carnitine	C26:0 Carnitine	[M+H]+	2	9,75	540.5002	**0,69**	**1,10**	2,4E-03	58%	UP

Fatty Acyl	Acyl-carnitine	18:1(OH) Carnitine	[M+H]+	5	5,10	442.3890	**1,08**	**1,62**	2,7E-03	51%	UP
Fatty Acyl	N-Acyl ethanolamide	24:0 FAE	[M+H]+	0	9,39	412.4149	**0,27**	**0,40**	1,8E-02	48%	UP
Sphingolipid	Ceramide	Cer(d18:1/18:1)	[M+H]+	3	10,95	564.5368	**7,11**	**10,51**	2,0E-02	48%	UP
Sphingolipid	Ceramide	Cer(d18:1/20:1)	[M+H]+	0	11,19	594.5842	**10,09**	**14,66**	7,9E-03	45%	UP
Fatty Acyl	N-Acyl ethanolamide	16:0 FAE	[M+H]+	1	4,64	300.2901	**9,25**	**13,38**	6,3E-03	45%	UP
Glycerolipid	Diacylglycerol	(34:3) DG	[M+H]+	2	10,01	591.4999	**0,54**	**0,78**	4,4E-02	44%	UP
Fatty Acyl	N-Acyl ethanolamide	17:0 FAE	[M+H]+	2	5,15	314.3061	**0,20**	**0,28**	2,4E-03	41%	UP
Sphingolipid	Ceramide	Cer(d18:1/20:0)	[M+H]+	0	11,45	592.5667	**0,22**	**0,30**	1,1E-02	38%	UP
Fatty Acyl	N-Acyl ethanolamide	18:0 FAE	[M+H]+	0	6,17	328.3213	**21,14**	**28,10**	1,4E-02	33%	UP
Fatty Acyl	Fatty Acid	18:4 FA	[M+Na]+	0	4,73	299.1984	**0,20**	**0,26**	2,1E-03	31%	UP
GlycerophospholipId	Lysophosphatidylcholine	LysoPC(14:0)	[M+H]+	0	1,91	468.3082	**0,35**	**0,25**	1,3E-03	-31%	DOWN
Fatty Acyl	Wax ester	Oleyl palmitoelate	[M+H]+	2	10,18	505.4994	**0,11**	**0,07**	3,2E-02	-31%	DOWN
GlycerophospholipId	Lysophosphatidylethanolamine	LysoPE(20:0)	[M+H]+	0	6,95	566.4182	**0,28**	**0,20**	5,6E-03	-31%	DOWN
GlycerophospholipId	Lysophosphatidylethanolamine	LysoPE(20:2)	[M+H]+	0	3,88	548.3711	**0,41**	**0,28**	2,8E-02	-32%	DOWN
Glycerolipid	Monoacylglycerol	18:0 MG	[M+Na]+	0	6,79	381.2974	**0,24**	**0,16**	3,1E-04	-34%	DOWN
Glycerolipid	Monoacylglycerol	24:0 MG	[M+H]+	4	9,69	443.4114	**3,73**	**2,41**	2,8E-02	-35%	DOWN
GlycerophospholipId	Lysophosphatidylethanolamine	LysoPE(20:4)	[M+H]+	3	2,27	442.3532	**0,56**	**0,36**	1,3E-03	-36%	DOWN
Glycerolipid	Monoacylglycerol	16:0 MG	[M+Na]+	0	5,40	353.2663	**0,25**	**0,16**	5,2E-04	-36%	DOWN
GlycerophospholipId	Lysophosphatidylcholine	LysoPC(20:3)	[M+H]+	2	4,86	546.3540	**5,41**	**3,40**	1,8E-05	-37%	DOWN
GlycerophospholipId	Lysophosphatidylcholine	LysoPC(20:4)	[M+H]+	4	3,54	544.3373	**0,26**	**0,16**	9,5E-03	-38%	DOWN
Glycerolipid	Diacylglycerol	(32:0) DG	[M-H2O+H]+	4	12,14	551.5063	**0,10**	**0,06**	2,3E-02	-39%	DOWN
GlycerophospholipId	Lysophosphatidylserine	LysoPS(O-20)	[M+H]+	1	3,69	540.3670	**0,21**	**0,13**	1,2E-03	-40%	DOWN
Glycerolipid	Monoacylglycerol	22:0 MG	[M+Na]+	0	8,88	437.3601	**0,34**	**0,20**	1,8E-05	-40%	DOWN
Glycerophosp	Lysophosphatidylch	LysoPC(P-18:1)	[M+H]+	0	4,85	506.3601	**0,17**	**0,10**	8,7E-04	-41%	DOWN

hoLipid	oline										
Glycerolipid	Diacylglycerol	(28:2) DG	[M+H]+	1	7,32	509.4195	**0,26**	**0,14**	2,1E-02	-44%	DOWN
Glycerophosphoslipid	Lysophosphatidylcholine	LysoPC(18:2)	[M-H2O+H]+	0	2,43	544.3403	**0,87**	**0,45**	3,3E-03	-48%	DOWN
Sphingolipid	Sphinganine	Sphinganine	[M+H]+	0	3,08	302.3055	**4,55**	**2,06**	4,6E-03	-55%	DOWN
Glycerolipid	Diacylglycerol	(36:4)DG	[M-H2O+H]+	0	10,47	599.5059	**2,79**	**1,18**	7,6E-03	-58%	DOWN
Glycerophosphoslipid	Lysophosphatidylcholine	LysoPC(18:0)	[M+H]+	1	4,53	524.3717	**3,70**	**1,54**	4,1E-05	-58%	DOWN
Glycerophosphoslipid	Lysophosphatidylcholine	LysoPC(22:4)	[M+H]+	0	3,26	572.3713	**0,25**	**0,10**	2,2E-06	-59%	DOWN
Glycerolipid	Diacylglycerol	(36:5)DG	[M-H2O+H]+	0	10,03	597.4881	**0,18**	**0,06**	4,7E-03	-65%	DOWN
Glycerophosphoslipid	Lysophosphatidylethanolamine	LysoPE(22:1)	[M+H]+	0	3,93	536.3715	**1,13**	**0,36**	1,1E-04	-68%	DOWN
Glycerophosphoslipid	Lysophosphatidylcholine	LysoPC(22:5)	[M+H]+	0	2,84	570.3545	**0,11**	**0,03**	1,8E-04	-71%	DOWN
Glycerophosphoslipid	Lysophosphatidic acid	16:0 PA	[M-H2O+H]+	1	3,31	393.2399	**0,27**	**0,07**	1,3E-03	-75%	DOWN
Glycerophosphoslipid	Lysophosphatidic acid	18:0 PA	[M-H2O+H]+	0	4,82	421.2716	**0,18**	**0,04**	5,8E-04	-80%	DOWN
Sphingolipid	Ceramide	Cer(d18:1/14:0)	[M-H2O+H]+	2	9,73	492.4795	**0,15**	**0,00**	7,5E-05	-100%	DOWN
Sterol Lipid	Cholesteryl ester	Cholesteryl acetate	[M+H]+	0	8,55	429.3728	**0,20**	**0,00**	7,7E-05	-100%	DOWN
Glycerolipid	Diacylglycerol	(16:0e/18:0) DG	[M-H2O+H]+	0	12,14	565.5550	**0,34**	**0,00**	1,4E-04	-100%	DOWN
Glycerolipid	Diacylglycerol	(34:1) DG	[M-H2O+H]+	3	10,37	577.5184	**0,31**	**0,00**	5,5E-04	-100%	DOWN
Glycerophosphoslipid	Lysophosphatidylcholine	LysoPC(22:6)	[M+H]+	0	2,26	568.3403	**0,39**	**0,00**	2,1E-02	-100%	DOWN

Target	Reference	1st	2nd	Mean
A_1 (*h*) (antagonist radioligand)	DPCPX	-0.1	10.6	5.3
A_{2A} (*h*) (agonist radioligand)	NECA	-6.4	2.5	-1.9
A_3 (*h*) (agonist radioligand)	IB-MECA	2.3	-11.4	-4.6
α_1 (non-selective) (antagonist radioligand)	Prazosin	-4.5	3.0	-0.8
α_2 (non-selective) (antagonist radioligand)	Yohimbine	-11.4	8.2	-1.6
β_1 (*h*) (agonist radioligand)	Atenolol	-1.7	1.4	-0.2
β_2 (*h*) (agonist radioligand)	ICI 118551	-14.4	-6.2	-10.3
AT_1 (*h*) (antagonist radioligand)	Saralasin	3.3	13.1	8.2
AT_2 (*h*) (agonist radioligand)	Angiotensin-II	-12.8	-6.4	-9.6
BZD (central) (agonist radioligand)	Diazepam	-9.2	-8.2	-8.7
B_1 (*h*) (agonist radioligand)	$desArg^{10}$-KD	-3.8	-4.8	-4.3
B_2 (*h*) (agonist radioligand)	NPC 567	0.6	-3.0	-1.2
CB_1 (*h*) (agonist radioligand)	CP 55940	-2.1	0.2	-1.0
CB_2 (*h*) (agonist radioligand)	WIN 55212-2	-8.9	6.8	-1.1
CCK_2 (CCKB) (*h*) (agonist radioligand)	CCK-8s	-3.7	-13.4	-8.6
CRF_1 (*h*) (agonist radioligand)	Sauvagine	-0.1	-4.0	-2.0
D_1 (*h*) (antagonist radioligand)	SCH 23390	1.1	-4.6	-1.8
D_{2S} (*h*) (antagonist radioligand)	(+)Butaclamol	28.4	56.5	42.4
D_3 (*h*) (antagonist radioligand)	(+)Butaclamol	-10.3	-16.5	-13.4
$D_{4.4}$ (*h*) (antagonist radioligand)	Clozapine	12.5	0.5	6.5
ETA (*h*) (agonist radioligand)	Endothelin-1	-3.0	-2.1	-2.5
ETB (*h*) (agonist radioligand)	Endothelin-3	2.4	-8.3	-2.9
GABA (non-selective) (agonist radioligand)	GABA	-0.1	-2.0	-1.1
AMPA (agonist radioligand)	L-glutamate	-3.3	-5.6	-4.4
kainate (agonist radioligand)	kainic	-9.6	-2.4	-6.0
NMDA (antagonist radioligand)	CGS 19755	2.9	17.1	10.0
H_1 (*h*) (antagonist radioligand)	Pyrilamine	6.0	1.4	3.7
H_2 (*h*) (antagonist radioligand)	Cimetidine	-4.8	-9.8	-7.3
H_3 (I) (agonist radioligand)	(R)α-Me-histamine	-2.4	-7.9	-5.1
I_2 (antagonist radioligand)	Idazoxan	-8.5	-7.9	-8.2
BLT_1 (LTB_4) (*h*) (agonist radioligand)	LTB4	7.0	4.7	5.8
$CysLT_1$ (LTD_4) (*h*) (agonist radioligand)	LTD4	16.0	13.9	14.9
MC_4 (*h*) (agonist radioligand)	NDP-α-MSH	-6.2	-3.7	-4.9
MT_1 (ML_{1A}) (*h*) (agonist radioligand)	Melatonin	9.4	4.4	6.9
M (non-selective) (antagonist radioligand)	atropine	-39.6	10.7	-14.4
NK_1 (*h*) (agonist radioligand)	$[Sar^9,Met(O_2)^{11}]$-SP	-16.2	-17.7	-16.9
NK_2 (*h*) (agonist radioligand)	$[Nleu^{10}]$-NKA	15.9	3.1	9.5
NK_3 (*h*) (antagonist radioligand)	SB 222200	-3.4	4.5	0.6
Y (non-selective) (agonist radioligand)	NPY	-23.5	7.0	-8.3
N neuronal α4β2 (*h*) (agonist radioligand)	Nicotine	1.0	-9.5	-4.2
opioid (non-selective) (antagonist radioligand)	Naloxone	47.1	21.4	34.3
NOP (ORL1) (*h*) (agonist radioligand)	Nociceptin	1.4	1.1	1.2
PPARγ (*h*) (agonist radioligand)	Rosiglitazone	-7.5	8.0	0.2
PCP (antagonist radioligand)	MK 801	13.2	6.9	10.0
EP_2 (*h*) (agonist radioligand)	PGE_2	3.1	-2.2	0.4
IP (PGI_2) (*h*) (agonist radioligand)	Iloprost	3.6	-8.7	-2.6
P2X (agonist radioligand)	α,β-MeATP	19.3	1.7	10.5
P2Y (agonist radioligand)	dATPαS	1.4	0.4	0.9
5-HT1, Non-Selective	Serotonin (5-HT)	-4.5	5.2	0.3
sigma (non-selective) (*h*) (agonist radioligand)	Haloperidol	-11.9	-3.3	-7.6
GR (*h*) (agonist radioligand)	Dexamethasone	-5.8	-11.1	-8.4
ER (non-selective) (*h*) (agonist radioligand)	17-β-estradiol	-27.5	-20.5	-24.0
PR (*h*) (agonist radioligand)	Promegestone	-11.0	-11.5	-11.2
AR (*h*) (agonist radioligand)	Mibolerone	-4.6	1.3	-1.7
TRH_1 (*h*) (agonist radioligand)	TRH	-12.5	3.8	-4.3
$V1_a$ (*h*) (agonist radioligand)	$[d(CH_2)_5{}^1,Tyr(Me)_2]$-AVP	2.1	7.3	4.7
V2 (*h*) (agonist radioligand)	AVP	-24.9	6.6	-9.1
Ca^{2+} channel (L, dihydropyridine site) (antagonist radioligand)	Nitrendipine	2.8	-2.5	0.2
Ca^{2+} channel (L, diltiazem site) (benzothiazepines) (antagonist radioligand)	Diltiazem	7.1	3.6	5.4
Ca^{2+} channel (L, verapamil site) (phenylalkylamine) (antagonist radioligand)	D 600	-7.1	0.1	-3.5
K_{ATP} channel (antagonist radioligand)	Glibenclamide	6.4	18.3	12.4
K_V channel (antagonist radioligand)	α-dendrotoxin	-8.8	-4.0	-6.4
SK_{Ca} channel (antagonist radioligand)	Apamin	11.3	-3.6	3.9
Na^+ channel (site 2) (antagonist radioligand)	Veratridine	12.0	3.9	8.0
Cl^- channel (GABA-gated) (antagonist radioligand)	Picrotoxinin	2.2	-3.3	-0.5
norepinephrine transporter (*h*) (antagonist radioligand)	Protriptyline	-9.2	-11.4	-10.3
dopamine transporter (*h*) (antagonist radioligand)	BTCP	-7.4	1.6	-2.9
GABA transporter (antagonist radioligand)	Nipecotic	-0.7	-7.0	-3.9
choline transporter (CHT1) (*h*) (antagonist radioligand)	Hemicholinium-3	-30.4	-25.2	-27.8

5-HT transporter (*h*) (antagonist radioligand)	Imipramine	-5.4	-2.0	-3.7
COX_1 (*h*)	Diclofenac	19.9	31.3	25.6
5-lipoxygenase (*h*)	NDGA	-2.4	15.2	6.4
PDE1B (*h*)	Nitrendipine	32.0	28.8	30.4
PDE2A1 (*h*)	EHNA	-0.3	0.6	0.1
PDE3A (*h*)	Milrinone	3.1	0.4	1.8
$PDE4D_2$ (*h*)	Rolipram	2.0	1.5	1.7
PDE5 (*h*) (non-selective)	Dipyridamole	-18.7	-6.1	-12.4
Protein Tyrosine Phosphatase, CDC25A	NSC663284	6.4	9.6	8.0
Protein Tyrosine Phosphatase, PTPN1 (PTP1B)	$(NH_4)_6Mo_7O_{24}$	0.0	-3.5	-1.8
PKCα (*h*)	Bis 10	0.5	-14.4	-7.0
acetylcholinesterase (*h*)	Neostigmine	-31.0	-28.1	-29.6
COMT	Ro 41-0960	30.1	28.6	29.4
GABA transaminase	*O*-(Carboxyméthyl) hydroxylamine hémihydrochloride	5.4	9.3	7.3
MAO-A (*h*)	Clorgyline	7.1	4.0	5.6
MAO-B (*h*) recombinant enzyme	Deprenyl	-16.5	-12.3	-14.4
Tyrosine Hydroxylase	alpha-Methyl-L-P-Tyrosine	-17.8	-23.7	-20.8
ATPase (Na^+/K^+)	Ouabain	-0.4	0.0	-0.2
CENP-E (*h*)	Rose bengal	6.6	3.6	5.1
Eg5 (*h*)	S-trityl-L-cysteine	4.4	4.0	4.2
HDAC3 (*h*)	Trichostatin	-3.5	-4.0	-3.7
HDAC4 (*h*)	Trichostatin	0.1	7.3	3.7
HDAC6 (*h*)	Trichostatin	-5.2	-8.2	-6.7
HDAC11 (*h*)	Scriptaid	-66.4	-79.7	-73.0
sirtuin 1 (*h*)	Suramin	1.2	-0.6	0.3
sirtuin 2 (*h*)	Suramin	-0.2	-0.8	-0.5
adenylyl cyclase	Forskolin	0.1	0.4	0.2
guanylyl cyclase (h)	Sodium	0.2	0.4	0.3

Table S3: Pharmacological profiling of NAT(20:0). The ability of NAT(20:0) (10 μM) to interact with a panel of human (*h*) receptors, ion channels, neurotransmitter transporters and enzymes was tested at our request, by contract research organization Eurofins SA (Le Bois l'Eveque, France). The table shows the target examined, the radioligands (in parenthesis) and reference compounds used, and the effect produced by NAT(20:0) in two independent tests (1st and 2nd). Results are expressed as percent of the effect produced by each reference compound. The average of those two values is also shown. We observed no relevant changes (arbitrarily set at ≥ 50% of control) for this set of targets

Abbreviations: AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; AR, androgen receptor; AT_1, AT_2, angiotensin receptor 1 and 2; A_1, A_{2a}, A_3, Adenosine receptor 1, 2a and 3; α_1, α_2, β_1, β_2, Adrenergic receptor α_1, α_2, β_1 and β_2; BLT_1, Leukotriene B_4 receptor 1; BZD, Benzodiazepine; B_1, B_2, bradykinin receptor 1 and 2; CB_1, CB_2, cannabinoid receptor 1 and 2; CCK , Cholecystokinin; CENP-E, Centromere-associated protein E; COMT, catechol- O-methyl transferase; Cox-1, cyclooxygenase-1; CRF_1, corticotropin-releasing factor; $CysLT_1$, Cysteinyl leukotriene receptor 1; D_1, D_{2s},D_3,$D_{4.4}$, dopamine receptor 1, 2s, 3 and 4.4; Eg5, mitotic kinesin; EP_2, prostaglandine E_2 receptor 2; ER, estrogen receptor; ET_A, ET_B, endothelin receptor A and B; GABA, ɣ-aminobutyric acid; GR, glucocorticoid receptor; HDAC3, HDAC4, HDAC6, HDAC11, histone deacetylase 3, 4, 6 and 11; H_1, H_2, H_3, histamine receptor 1, 2 and 3; 5-HT, serotonin receptor; IP, prostacyclin receptor; I_2, imidazoline receptor 2; M, muscarinic receptor; MAO-A, MAO-B, monoamine oxidase A and B; MC_4, melanocortin-4 receptor; MT_1, melatonin receptor 1; N neuronal $\alpha_4\beta_2$, $\alpha_4\beta_2$ nicotinic acetylcholine receptor; NK_1, NK_2, NK_3, neurokinin receptor 1, 2 and 3; NMDA, *N*-methyl-D-aspartate receptor; NOP, nociceptin receptor; PCP, 1-(1-phenylcyclohexyl)piperidine; PDE1B, PDE2A1, PDE3A, PDE4D2, PDE5, phosphodiesterase 1B, 2A1, 3A, 4D2 and 5; PKCα, protein kinase C α; PPARγ, peroxisome proliferator-activated receptor gamma; PR, progesterone receptor; P2X, purinoceptor subtype 2 subtype X; P2Y, purinoceptor subtype 2 subtype Y**;** TRH1, thyrotropin-releasing hormone receptor; V_{1a}, V_2, vasopressin receptor 1a and 2; Y, neuropeptide Y receptor.