Supplementary information

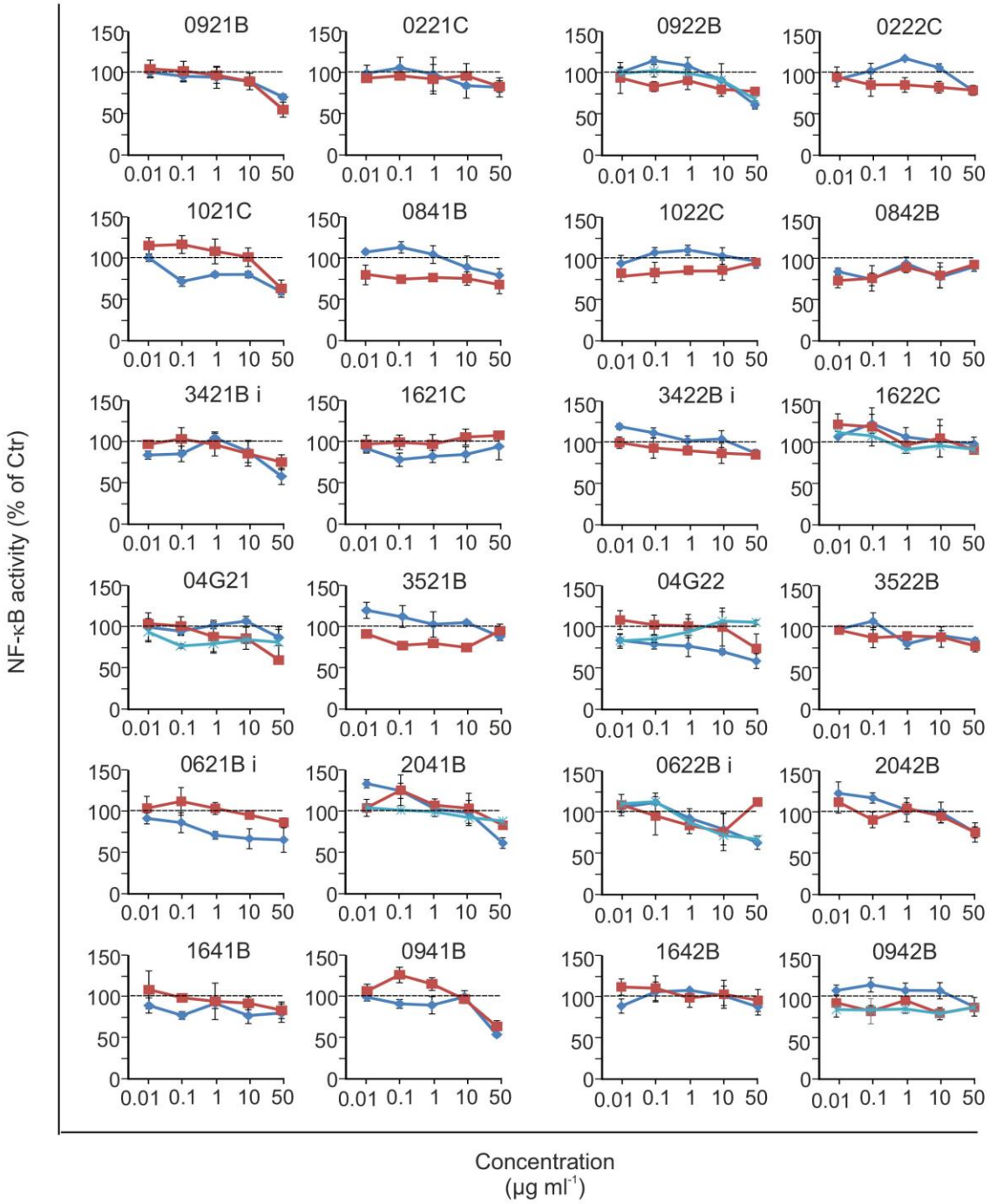


Figure S1. Validation of primary hits. Dose-dependent effects on NF-κB luciferase reporter activities of the selected algal extracts in TNFα-stimulated HaCaT cells. NF-κB activity in DMSO-treated cells is normalized to 100%. Each curve represents an independent experiment. Values are mean ± SD of technical replicates (n = 3); Ctr, control (DMSO + TNFα).

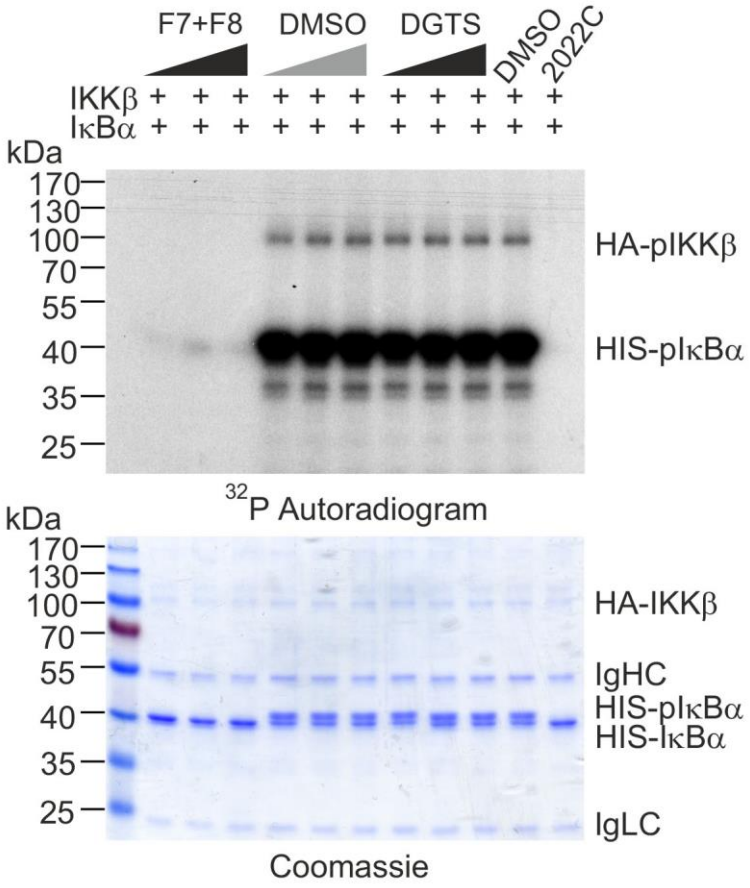


Figure S2. The active NAE_2022C fraction (F7+F8), but not DGTS, directly inhibits IKKβ kinase activity. IKKβ activity was analyzed by *in vitro* kinase assay using recombinant HIS-IκBα and [ϒ-^{32}P]ATP in the presence of DMSO, (F7+F8) fraction or DGTS (1, 10, 100 μM). The reactions were run on SDS-PAGE and analyzed by autoradiography; IgHC, immunoglobulin heavy chain; IgLC, immunoglobulin light chain.

Figure 3B
WB: anti-IκBα

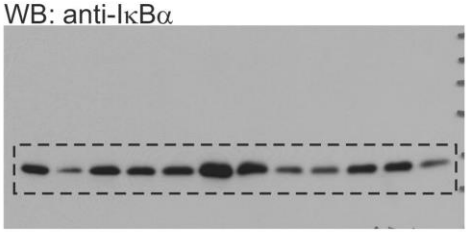


Figure 3B
WB: anti-β-Actin

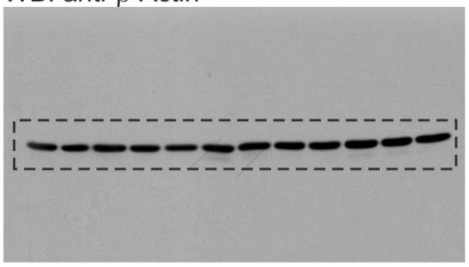


Figure 3B
WB: anti-pIκBα

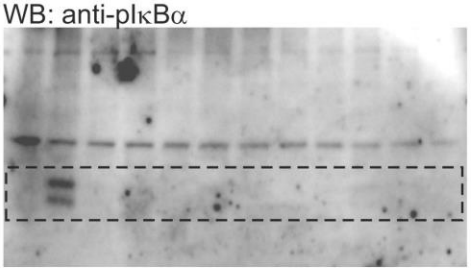


Figure 3B
WB: anti-β-Actin

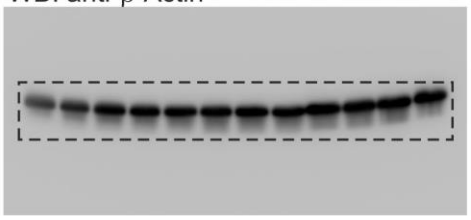


Figure 4A
WB: anti-IκBα

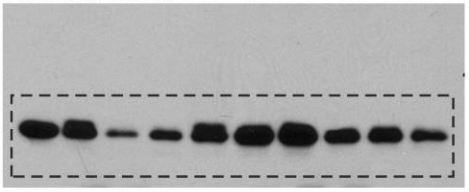


Figure 4A
WB: anti-pIκBα

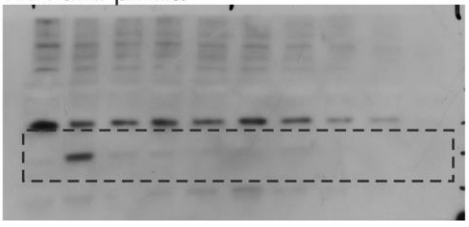


Figure 4A
WB: anti-pp38

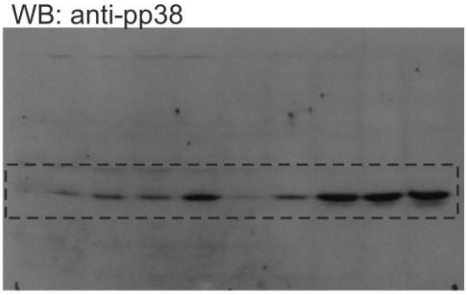


Figure 4A
WB: anti-β-Actin

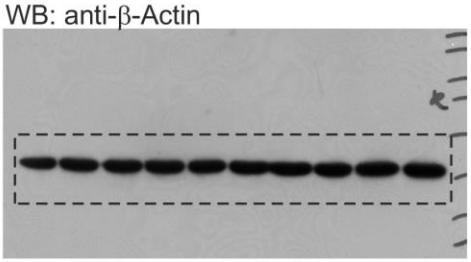


Figure 4A
WB: anti-pJNK

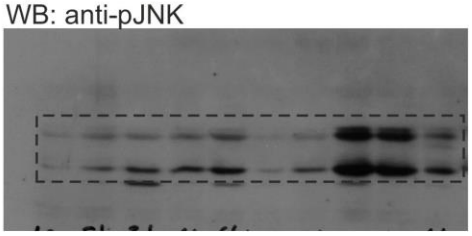


Figure 4A
WB: anti-β-Actin

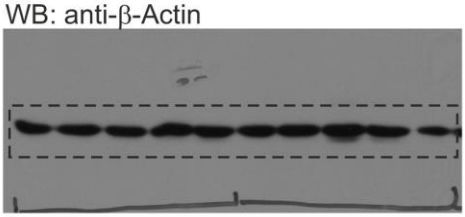


Figure 4A
WB: anti-pERK1/2

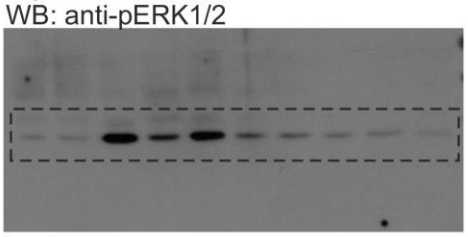


Figure 4A
WB: anti-β-Actin

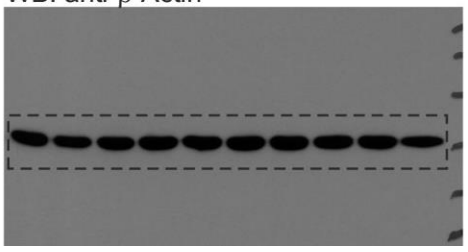


Figure S3. Original images. *Dashed line designates the cropped area.*

Table S1. List of algae strains selected from the ASIB 505 collection.

Algae Species	Collection ID	Growth in 3N-BBM	PAE ID	NAE ID
Subphylum: Chlorophytina	IB459	+++	0121	0122
			0141	0142
Coccomyxa subellipsoidea	BS110	+++	0221	0222
			0241	0242
Klebsormidium subellipsoidea or Interphylum subellipsoidea	IB505	+++	0321	0322
Chromochloris zofingiensis Order: Sphaeropleales	V46	+	04G21	04G22
			04G51	04G52
Xanthophyceae	V168	+++	0521	0522
n.a.	IB514	+++	0621	0622
			0641	0642
Coccomyxa subellipsoidea	T3	+++	0721	0722
Pseudochlorella subsphaerica Family: Prasiolaceae	BS775	+++	0821	0822
			0841	0842
Coccomyxa subellipsoidea Family: Coccomyxaceae	IB273 (PUFA)	+++	0921	0922
			0941	0942
Neocystis brevis Subphylum Chlorophytina	IB410	+++	1021	1022
Bracteacoccus subellipsoidea	V103	+++	1121	1122
	V219		1221	1222
Ectocarpus siliculosus Family: Ectocarpaceae	V50	+++	1321	1322
Pseudostichococcus subellipsoidea, Phylum: Chlorophyta	SAG 379 1c	+++	1411	1412
Trebouxiophyceae subellipsoidea	IB423	+++	1521	1522
Chromochloris zofingiensis Order: Sphaeropleales	IB408	+++	1621	1622
			1641	1642
Chlorella saccharophila	CV. Vulgaris	+++	1721	1722
			1741	1742
Diplosphaera subellipsoidea, Subphylum: Chlorophytina	T61	++	1821	1822
Bracteococcus subellipsoidea	V195	+	1921	1922
Chromochloris zofingiensis Subphylum: Chlorophytina	V142	+++	2021	2022
			2041	2042
Edaphochlorella mirabilis	IB407 (PUFA)	+++	2121	2122
			2131	2132

			2141	2142
n.a.	V6	+++	2221	2222
Bracteacoccus subellipsoidea	T87	+++	2321	2322
Scenedesmus subellipsoidea	V21	+	2411	2412
Dictyococcus varians *Order: Sphaeropleales*	V204	+++	2521 2551	2522 2552
Coccomyxa subellipsoidea	IB256	+	2611 2641	2612 2642
Coccomyxa subellipsoidea	V199	+++	2721	2722
Muriella subellipsoidea	BS319	+++	2811	2812
n.a.	V24	+	2911	2912
Ettila texensis	SAG 79.80	+++	3021	3022
Bracteacoccus subellipsoidea	V208	+	3111	3112
n.a.	CCALA 496	++	3221	3222
Coelastrella subellipsoidea Subphylum Chlorophytina	CH	+	3321	3322
Nostoc subellipsoidea	BS363	+++	3421	3422
Bracteacoccus subellipsoidea	V208	+++	3521	3522
Vischeria helvetica *Order: Eustigmatales*	V39	+	3611	3612

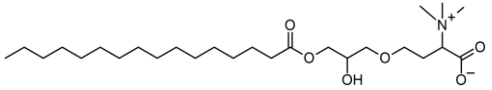
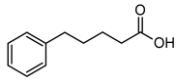
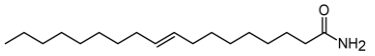
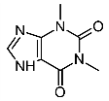
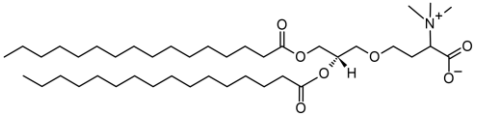
Table S2. Cytotoxicity of selected algae extracts

Extract ID	Cell viability (% of control)			
	0.1	1	10	100
	(μg ml^{-1})			
0121B i	100 ± 6	102 ± 7	102 ± 9	98 ± 9
0141B	102 ± 3	89 ± 8	96 ± 2	103 ± 2
0221C	102 ± 5	103 ± 5	102 ± 4	93 ± 1
0241C	101 ± 1	101 ± 2	99 ± 2	99 ± 6
0321B	101 ± 2	102 ± 1	102 ± 1	97 ± 1
04G21	105 ± 8	109 ± 11	106 ± 8	92 ± 1
04G51	100 ± 1	102 ± 1	101 ± 2	88 ± 5
0521B	102 ± 1	99 ± 1	99 ± 2	92 ± 4
0621B i	104 ± 7	102 ± 1	105 ± 7	86 ± 4
0641B	102 ± 6	102 ± 2	101 ± 3	97 ± 2
0721B	107 ± 6	109 ± 4	111 ± 4	110 ± 3
0821B i	104 ± 2	103 ± 1	104 ± 1	78 ± 10
0841B	102 ± 4	100 ± 2	97 ± 1	76 ± 4
0921B	101 ± 2	104 ± 4	102 ± 3	96 ± 4
0941B	101 ± 3	100 ± 4	99 ± 5	97 ± 2
1021C	101 ± 2	102 ± 5	99 ± 2	68 ± 2
1121C	100 ± 5	98 ± 2	96 ± 3	86 ± 3
1221B	97 ± 1	98 ± 3	96 ± 3	90 ± 2
1321B	102 ± 2	102 ± 1	101 ± 4	91 ± 3
1411B	103 ± 5	102 ± 6	102 ± 2	98 ± 2
1521B	103 ± 3	103 ± 2	104 ± 4	101 ± 2
1621C	103 ± 3	103 ± 4	104 ± 2	55 ± 2
1641B	102 ± 3	102 ± 1	100 ± 2	97 ± 2
1721C	102 ± 2	103 ± 3	103 ± 4	95 ± 2
1741B	100 ± 4	104 ± 3	101 ± 4	99 ± 1
1821B	102 ± 5	101 ± 3	100 ± 1	89 ± 3
1921C	102 ± 3	101 ± 2	102 ± 2	92 ± 1
2021C	101 ± 3	100 ± 2	102 ± 3	93 ± 3
2041B	102 ± 2	100 ± 1	101 ± 3	99 ± 2
2121B i	102 ± 1	101 ± 2	101 ± 1	94 ± 1
2131B	100 ± 4	103 ± 3	98 ± 2	89 ± 2
2141B	105 ± 2	102 ± 2	100 ± 6	90 ± 7
2221B	102 ± 1	99 ± 1	98 ± 4	90 ± 6
2321C	100 ± 4	102 ± 2	98 ± 3	90 ± 2
2411B	104 ± 2	103 ± 1	98 ± 3	96 ± 3
2521C	107 ± 3	103 ± 5	109 ± 4	96 ± 7
2551B	99 ± 1	94 ± 6	95 ± 3	89 ± 4

2611B	108 ± 3	106 ± 3	108 ± 2	97 ± 5
2641B	100 ± 1	100 ± 4	101 ± 3	99 ± 2
2721B	105 ± 2	110 ± 4	105 ± 5	95 ± 3
2811C	101 ± 3	103 ± 2	102 ± 4	99 ± 4
2911B	100 ± 4	102 ± 1	102 ± 5	99 ± 1
3021B	102 ± 3	103 ± 1	105 ± 4	92 ± 3
3111B	108 ± 2	108 ±4	109 ± 2	104 ± 3
3221B	101 ± 4	102 ± 3	103 ± 4	98 ± 3
3321C	105 ± 2	106 ± 2	102 ± 3	100 ± 2
3421B i	103 ± 3	102 ± 2	99 ± 2	99 ± 4
3521B	103 ± 2	100 ± 4	102 ± 4	98 ± 4
3611B	92 ± 2	92 ± 2	95 ± 2	72 ± 3
0122B i	98 ± 4	99 ± 4	96 ± 5	94 ± 2
0142B	103 ± 3	103 ± 5	104 ± 2	95 ± 3
0222C	101 ± 5	102 ± 3	103 ± 3	102 ± 4
0242C	94 ± 3	97 ± 2	94 ± 2	96 ± 4
0322B	97 ± 4	102 ± 2	99 ± 5	92 ± 5
04G22	105 ± 4	99 ± 3	105 ± 2	98 ± 3
04G52	103 ± 5	103 ± 7	99± 6	92 ± 3
0522B	102 ± 2	103 ± 3	104 ± 5	93 ± 2
0622B i	104 ± 3	101 ± 2	98 ± 2	94 ± 1
0642B	103 ± 1	102 ± 3	100 ± 4	101 ± 2
0722B	101 ± 2	100 ± 1	101 ± 2	92 ± 3
0822B i	102 ± 3	110 ± 5	106 ± 4	104 ± 2
0842B	95 ± 4	94 ± 4	97 ± 3	95 ± 2
0922B	95 ± 5	96 ± 2	98 ± 2	80 ± 3
0942B	91 ± 6	100 ± 4	99 ± 5	89 ± 4
1022C	93 ± 2	98 ± 4	101 ± 1	100 ± 4
1122C	102 ± 2	101 ± 1	104 ± 2	103 ± 2
1222B	100 ± 2	103 ± 2	104 ± 3	101 ± 3
1322B	99 ± 1	104 ± 1	103 ± 3	100 ± 4
1412B	98 ± 5	98 ± 3	103 ± 4	89 ± 3
1522B	100 ± 3	102 ± 2	104 ± 1	102 ± 2
1622C	106 ± 1	108 ± 2	108 ± 1	102 ± 2
1642B	102 ± 3	98 ± 2	103 ± 4	96 ± 7
1722C	105 ± 1	108 ± 2	107 ± 1	109 ± 3
1742B	100 ± 1	101 ± 5	101 ± 4	95 ± 5
1822B	105 ± 4	102 ± 4	103 ± 5	99 ± 2
1922C	100 ± 2	101 ± 3	100 ± 1	96 ± 2
2022C	100 ± 1	101 ± 3	103 ± 2	99 ± 2
2042B	100 ± 4	99 ± 3	101 ± 2	97 ± 5
2122B i	100 ± 1	102 ± 3	105 ± 2	104 ± 3

2132B	100 ± 4	104 ± 3	103 ± 5	105 ± 3
2142B	100 ± 1	101 ± 3	99 ± 2	95 ± 2
2222B	102 ± 4	98 ± 4	90 ± 2	89 ± 4
2322C	100 ± 4	104 ± 3	103 ± 5	105 ± 3
2412B	102 ± 3	99 ± 1	101 ± 3	98 ± 5
2522C	101 ± 2	99 ± 3	102 ± 2	94 ± 2
2552B	102 ± 1	101 ± 3	103 ± 2	98 ± 4
2612B	93 ± 5	95 ± 5	95 ± 4	98 ± 7
2642B	96 ± 3	95 ± 2	96 ± 4	97 ± 3
2722B	95 ± 6	96 ± 4	100 ± 2	75 ± 4
2812C	97 ± 2	96 ± 2	99 ± 1	94 ± 2
2912B	100 ± 5	102 ± 6	99 ± 1	95 ± 3
3022B	97 ± 1	95 ± 2	98 ± 2	97 ± 2
3112B	102 ± 3	105 ± 2	98 ± 3	94 ± 7
3222B	91 ± 2	89 ± 2	96 ± 2	103 ± 2
3322C	100 ± 2	101 ± 3	99 ± 1	94 ± 2
3422B i	100 ± 3	98 ± 5	99 ± 4	98 ± 2
3522B	99 ± 3	102 ± 3	98 ± 7	95 ± 4
3612B	94 ± 2	94 ± 2	95 ± 3	94 ± 4

Table S3. UHPLC-qTOF-MS/MS analysis of NAE_2022C active fraction (F7+F8)

Compound	Molecular formula	RT [min]	Calculated m/z $[M+H]^+$	Experimental m/z $[M+H]^+$	Δm/z [ppm]	Δm/z [mDa]	Structure
LDGTS 16:0	C26H51NO6	6.28	473.373	474.381	3.888	1.844	
5-Phenylvaleric acid	C11H14O2	9.16	178.099	179.106	4.849	0.869	
Oleamide	C18H35NO	10.08	281.273	282.280	1.954	0.552	
Theophylline	C7H8N4O2	10.57	180.081	181.088	0.995	0.194	
DGTS 32:0; DGTS 16:0-16:0	C42H81NO7	11.43	712.612	712.619	0.768	0.424	
DGTS 34:0; DGTS 16:0-18:0	C44H85NO7	11.41	739.636	740.643	3.911	2.896