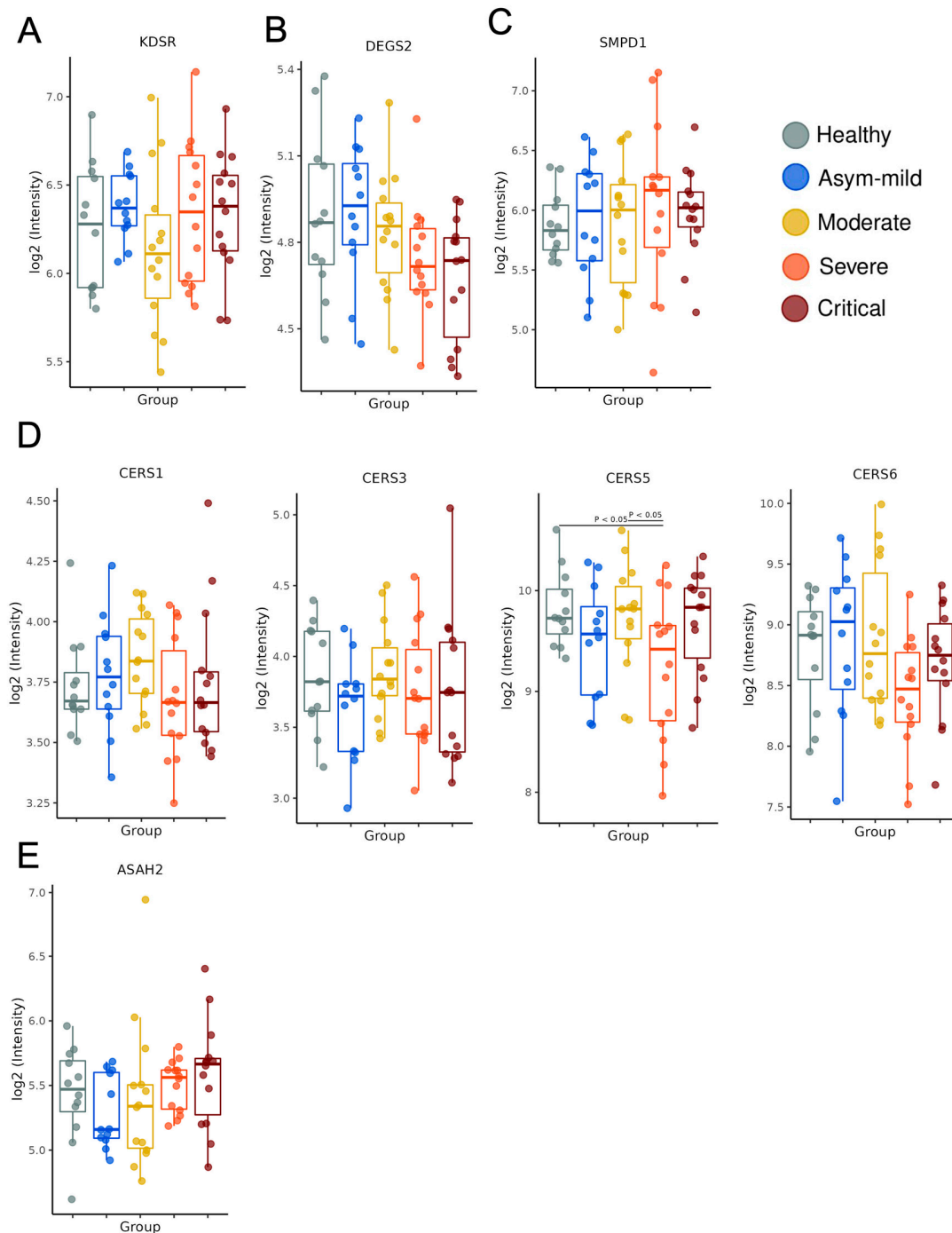*cells*

MDPI

Supplementary Material

Plasma Sphingomyelin Disturbances: Unveiling Its Dual Role as a Crucial Immunopathological Factor and a Severity Prognostic Biomarker in COVID-19

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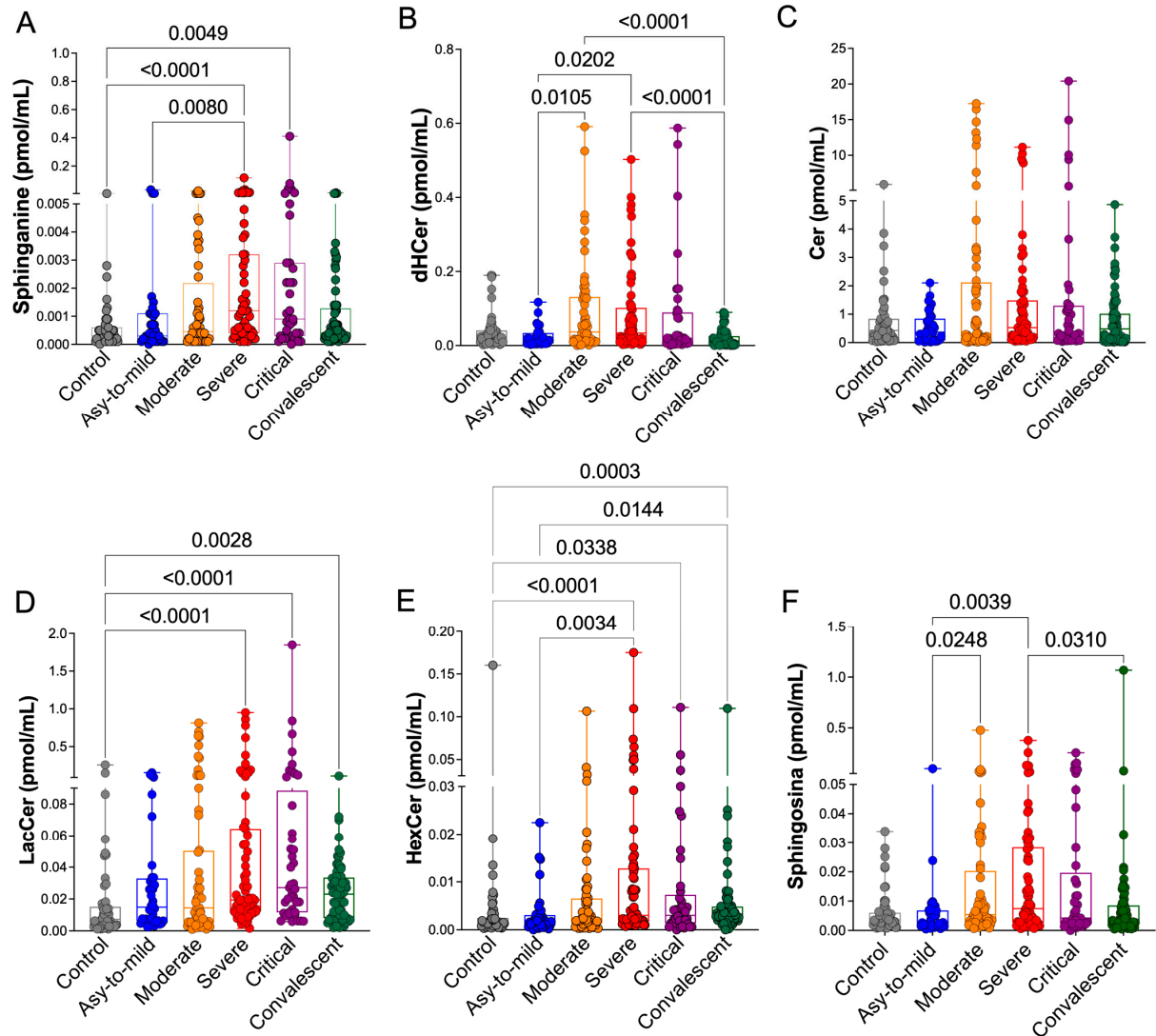
* Correspondence: Carlos A. Sorgi - carlos.sorgi@usp.br +55 16 3315-9176
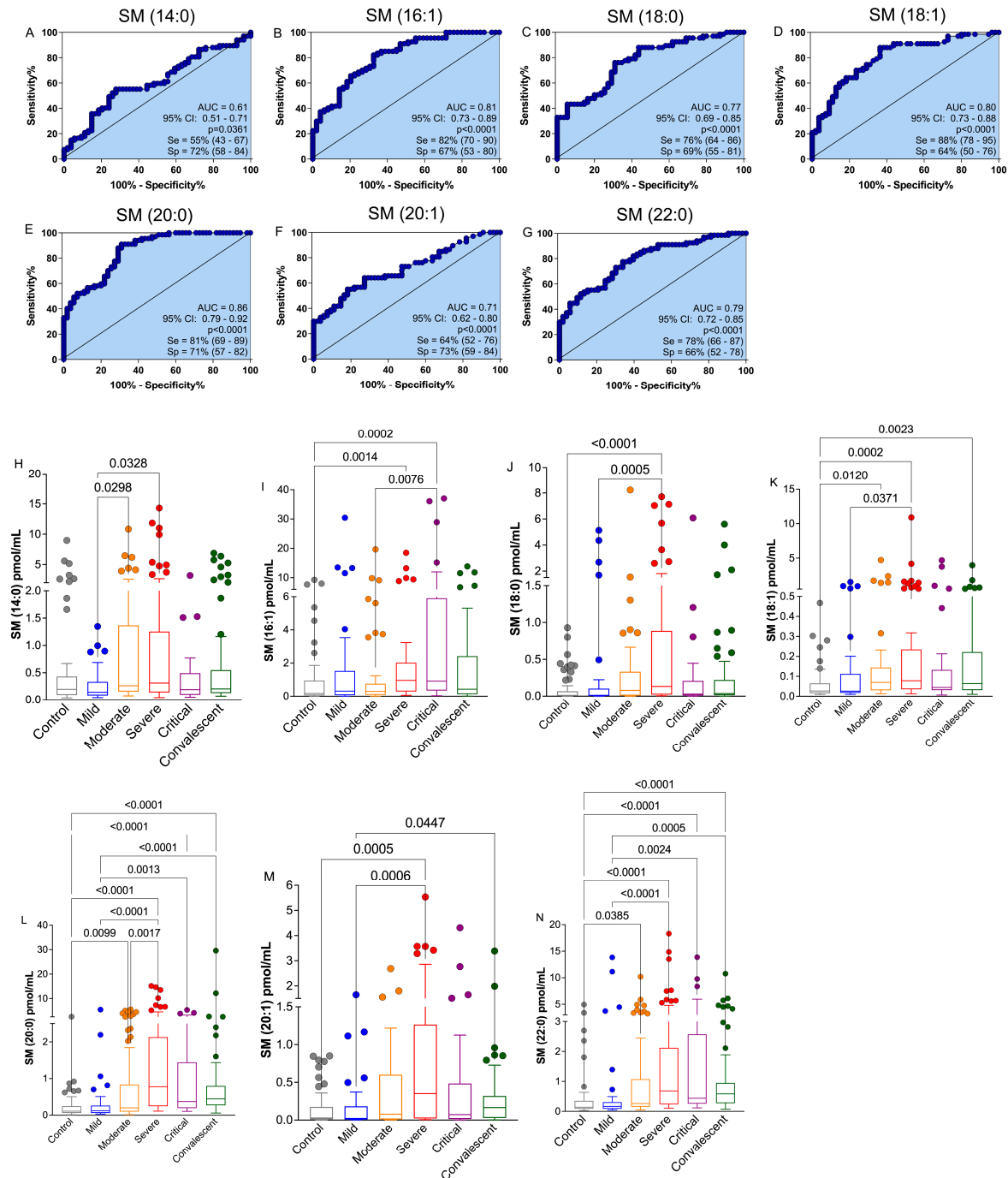[†] These authors contributed equally to this work and share first authorship
[#] These authors contributed equally to this work and share senior authorship
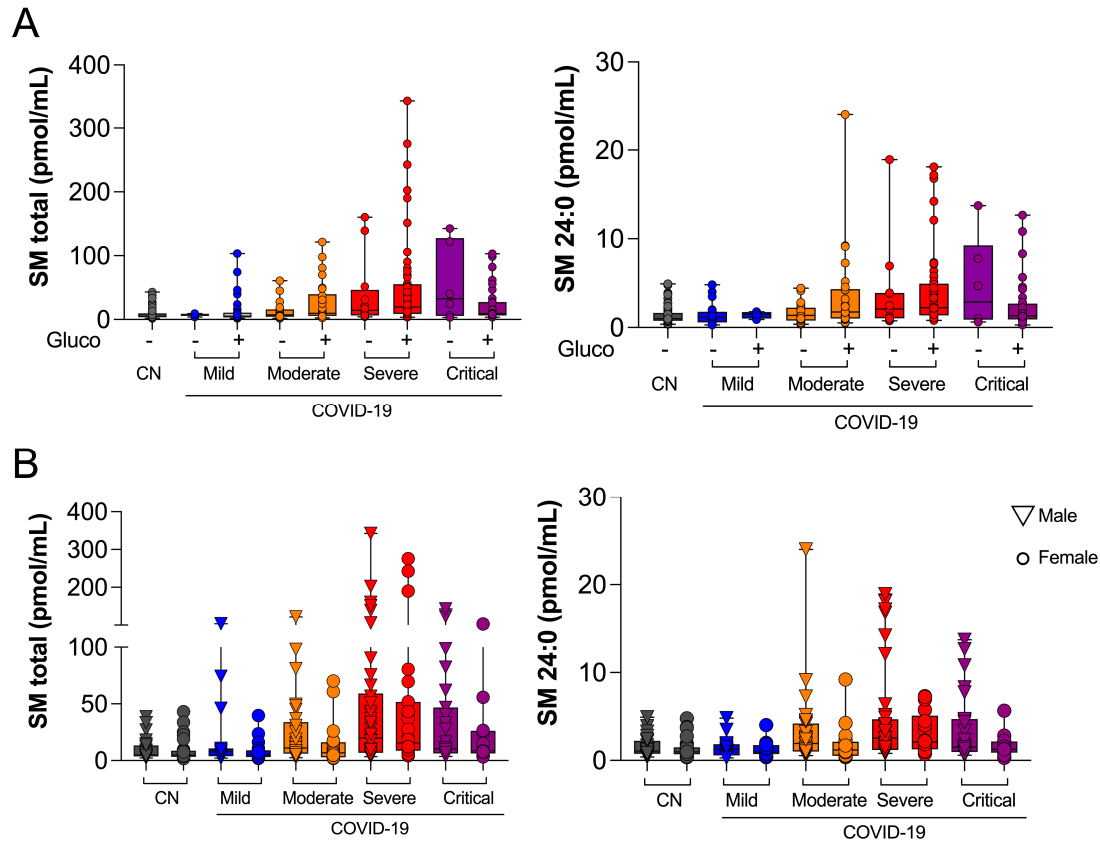
Supplementary Figure S1. Expression of sphingolipid metabolic enzymes in patients with COVID-19 according to severity. (**A**) 3-ketodihydrosphingosine reductase (*KDSR*), (**B**) Sphingolipid delta (4)-desaturase DES2 (*DEGS2*), (**C**) Sphingomyelin phosphodiesterase (*SMPD* 1), (**D**) Ceramide synthase 1, 3, 4, 5 (*CERS1*/3/5/6), (**E**) N-acylsphingosine amidohydrolase 2 (ASAH2), in: Control (n=12), Asy-to-mild (n=12), moderate (n=14), severe (n=14) and critical (n=14). The log2 of normalized gene expression profiles for analyzed groups at are showed as boxplots. Significant differences in transcript expression correspond to Benjamini and Hockberg adjusted p-values obtained from whole transcriptome differential expression analysis considering a threshold of < 0.05 in at least one pair of clinical groups. Details of enzyme nomenclatures Supplementary Table 4.

Supplementary Figure S2. Sphingolipids abundance profile in patients with COVID-19. LC–MS/MS measurements for (**A**) Sphinganine (18:0), (**B**) dihydroceramide (dHCer), (**C**) Ceramide (Cer), (**D**) Lactosylceramide 16:0 (LacCer), (**E**) Hexaglycosylceramide (HexCer) and (**F**) Sphingosine. Statistical analyzes were performed using the Kruskal-Wallis multiple comparison test (non-parametric), followed by the Dunn post-test for pairwise comparison. Data are expressed as median in boxplot graphics. Significance levels shown are based on statistically significant between groups with *p*-value < 0.05.

Supplementary Figure S3. ROC curves and Analysis of serum abundance sphingomyelin (SM) species (14:0), (16:1), (18:0), (18:1), (20:0), (20:1) and (22:0) in COVID-19. (A-G) ROC curves for sphingomyelin species (SM) in patients with severe forms of Covid-19. The curves compare the severe patients groups (n= 67) with the control (n=55). AUC: area under the curve; Se: sensitivity; Sp: specificity; CI: 95% confidence interval. (**H-N**) sphingomyelin class profile in control subjects compared to patients with COVID-19 and convalescents in: mild (n=36), moderate (n=60), severe (n=67), critical (n=41) and Convalescent individuals (n=77). Statistical analyzes were performed using the Kruskal-Wallis multiple comparison test (non-parametric), followed by the Dunn post-test for pairwise comparison. Data are expressed as median in boxplot graphics with minimum and maximum values. Significance levels shown are based on statistically significant between groups with *p*-value < 0.05.

Supplementary Figure S4. Glucocorticoid therapy and sex differences have no impact on total SM and (24:0)-specie production. Analysis of total sphingomyelin and SM (24:0) levels in relation to the use of (**A**) glucocorticoids and (**B**) male and female sex. Statistical analyzes were performed using the Kruskal-Wallis multiple comparison test (non-parametric), followed by the Dunn post-test for pairwise comparison. Data are expressed as median in boxplot graphics. Significance levels shown are based on statistically significant between groups with *p*-value < 0.05.

$$(I)\ AUC_{n(k)total} =\ AUC_{n(k)}\left(1 + 0.0109n + \frac{0.0109^2 n(n-1)}{2}\right)$$

$$(II)\ C_{lipid} = \frac{AUC_{lipid}}{AUC_{IS}} * C_{IS}$$

Supplementary Figure S5. Lipid quantification using internal standard and monoisotopic correction. (I) Monoisotopic correction: $AUC_{n(k)}$ total = corrected analyte area under the curve, $AUC_{n(k)}$ = quantified analyte monoisotopic mass area under the curve, n = number of C atoms, k = number of double bonds, **(II)** Lipid quantification based on the internal standard: C_{lipid} = analyte concentration (pmol/mL), AUC_{lipid} = monoisotopically corrected analyte area under the curve by Equation I ($AUC_{n(k)total}$), AUC_{IS} = area under the curve of internal standard corresponding to the analyte family, C_{IS} = internal standard concentration according to the Certificate of Analysis (Lot Number: LM6004-LM40-112A, Avanti Polar Lipids) [29].

Supplementary Table S1: Sphingolipid subclasses and species detected in our cohort.

Subclasses	Number of species	Species Description
Ceramide	9	Cer (16:0), Cer (18:0), Cer (18:1), Cer (20:0), Cer (22:0), Cer (23:0), Cer (24:0), Cer (24:1), Cer (25:0)
Sphingosine	2	Sphingosine (14:0), Sphingosine (18:0)
Sphinganine	1	Sphinganine (18:0)
Sphingomyelin (SM)	17	SM (14:0), SM (16:0), SM (16:1), SM (18:0), SM (18:1), SM (20:0), SM (20:1), SM (22:0), SM (22:1), SM (23:0), SM (23:1), SM (24:0), SM (24:1), SM (25:0), SM (25:1), SM (26:0), SM (26:1).
Hexaglycosylceramide (HexCer)	2	HexCer (16:0), HexCer (24:0)
Lactosylceramide (LacCer)	2	LacCer (16:0), LacCER(d18:1/14:0)
Dihydroceramide (dHCer)	5	dHCer(d18:0/16:0), dHCer(d18:0/18:0), dHCer(d18:0/24:0), dHCer(d20:0/16:0), dHCer(d20:0/22:0)
Total	38	

Supplementary Table S2. Target high-resolution mass spectrometry parameters for SL species.

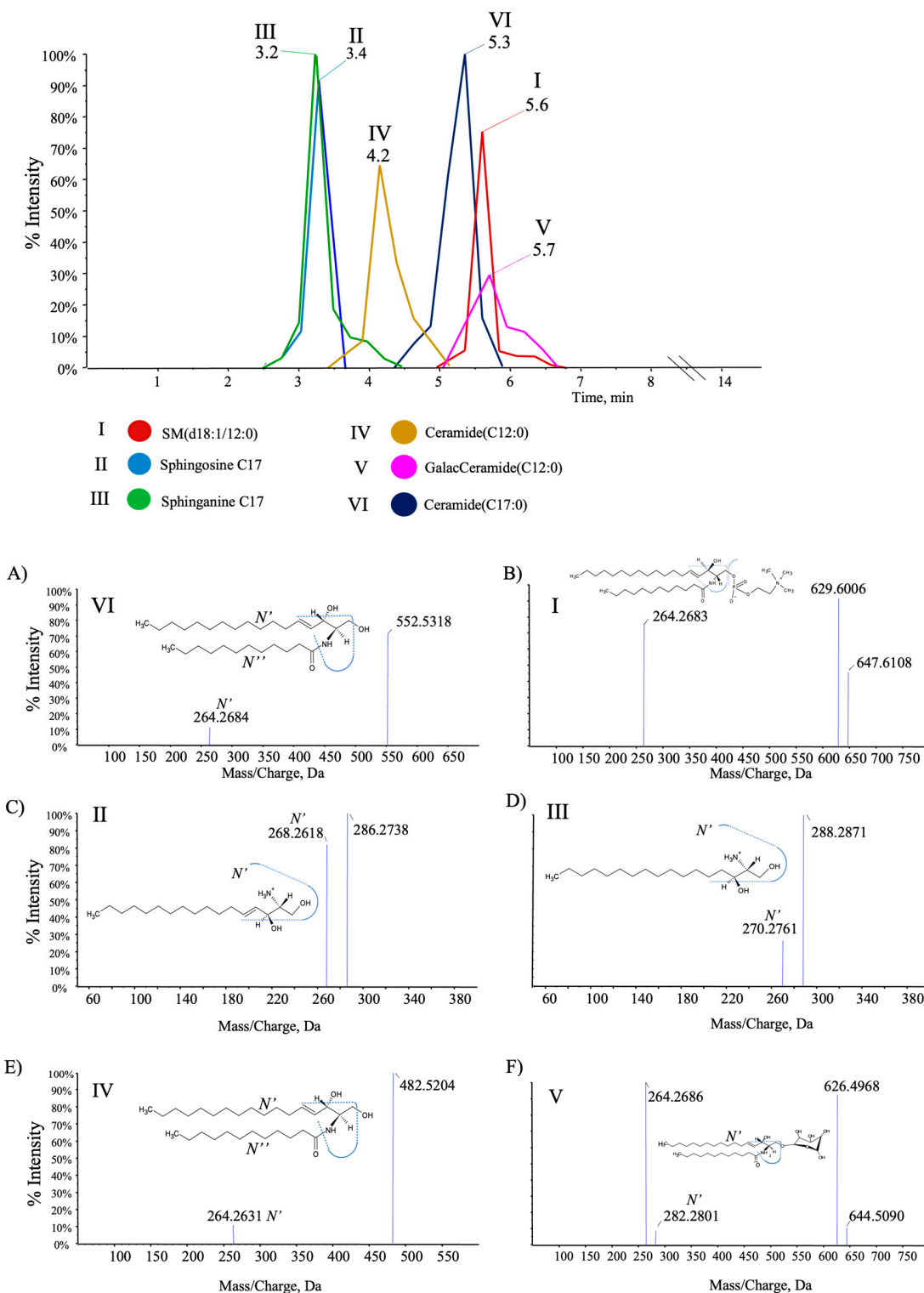| Experiment	Precursor ion (m/z)	Analyte	Internal Standard	Fragment ion (m/z)
1	100-2000	TOF-MS (untargeted)	-	-
2	552,5	Ceramide (d18:1/17:0)	IS	534.5237-534.5297
3	647,5	SM (d18:1/12:0)	IS Mix II (Avanti)	184.0703-184.0753
4	286,2	Sphingosine C17:0	IS Mix II (Avanti)	268.2623-268.2663
5	288,2	Sphinganine C17:0	IS Mix II (Avanti)	270.2750-270.2810
6	368,2	Sphinganine-1-P C17:0	IS Mix II (Avanti)	270.2750-270.2830
7	482,4	Ceramide (d18:1/12:0)	IS Mix II (Avanti)	264.2653-264.2703
8	644,5	GlcCer (d18:1/12:0)	IS Mix II (Avanti)	264.2652-264.26702
9	806,5	LacCer (d18:1/12:0)	IS Mix II (Avanti)	264.2652-264.26702
10	538,5	Ceramide (d18:1/16:0)	Ceramide (d18:1/12:0)	264.2652 - 264.26710
11	566,5	Ceramide (d18:1/18:0)	Ceramide (d18:1/12:0)	264.2652 - 264.26704
12	648,6	Ceramide (d18:1/24:1)	Ceramide (d18:1/12:0)	264.2652 - 264.26802
13	650,6	Ceramide (d18:1/24:0)	Ceramide (d18:1/12:0)	264.2652 - 264.26702
14	664,4	Ceramide (d18:1/25:0)	Ceramide (d18:1/12:0)	264.2652 - 264.26702
15	700,5	GlcCer (d18:1/16:0)	GlcCer (d18:1/12:0)	264.2652 - 264.26702
16	728,6	GlcCer (d18:1/18:0)	GlcCer (d18:1/12:0)	264.2652 - 264.26702
17	810,6	GlcCer (d18:1/24:1)	GlcCer (d18:1/12:0)	264.2652 - 264.26702
18	731,6	SM (d18:1/18:0)	SM (d18:1/12:0)	184.0703 - 184.0753
19	815,7	SM (d18:1/24:0)	SM (d18:1/12:0)	184.0703 - 184.0753
20	862,6	LacCer (d18:1/16:0)	LacCer (d18:1/12:0)	264.2652 - 264.26702
21	974,7	LacCer (d18:124:0)	LacCer (d18:1/12:0)	264.2652 - 264.26702
22	300,3	Sphingosine C18:0	Sphingosine C17:0	282.2480 - 282.2530
23	272,2	Sphingosine C16:0	Sphingosine C17:0	254.2164 - 254.2214
24	244,2	Sphingosine C14:0	Sphingosine C17:0	226.1765 - 226.1815
25	302,2	Sphinganine C18:0	Sphinganine C17:0	284.2912 - 284.2952
26	274,2	Sphinganine C16:0	Sphinganine C17:0	256.2612 - 256.2652
27	382,2	Sphinganine-1-P C18:0	Sphinganine-1-P C17:0	364.2120 - 364.2160
28	354,2	Sphinganine-1-P C16:0	Sphinganine-1-P C17:0	336.2298 - 336.2338
29	356,35	Sphingosine C22:1	Sphingosine C17:0	338.3500 - 338.3540
30	328,3	Sphingosine C20:1	Sphingosine C17:0	310.3000 - 310.3040
31	330,3	Sphinganine C20:0	Sphinganine C17:0	214.3000 - 214.3040
32	410,3	Sphinganine-1-P C20:0	Sphinganine C17:0	392.3000 - 392.3040
33	464,4	Ceramide (d18:1/18:1)	Ceramide (d18:1/12:0)	264.2694 - 264.2714
34	594,6	Ceramide (d18:1/20:0)	Ceramide (d18:1/12:0)	264.2671 - 264.2701
35	622,7	Ceramide (d18:1/22:0)	Ceramide (d18:1/12:0)	264.2671 - 264.2701

36	*634,7*	Ceramide (d18:1/23:1)	*Ceramide (d18:1/12:0)*	*264.2671 - 264.2701*
37	*636,7*	Ceramide (d18:1/23:0)	*Ceramide (d18:1/12:0)*	*264.2671 - 264.2701*
38	*662,8*	Ceramide (d18:1/25:1)	*Ceramide (d18:1/12:0)*	*264.2671 - 264.2701*
39	*676,8*	Ceramide (d18:1/26:1)	*Ceramide (d18:1/12:0)*	*264.2671 - 264.2701*
40	*678,8*	Ceramide (d18:1/26:0)	*Ceramide (d18:1/12:0)*	*264.2671 - 264.2701*
41	*675,5*	SM (d18:1/14:0)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
42	*701,6*	SM (d18:1/16:0)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
43	*703,57*	SM (d18:1/16:0)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
44	*729,6*	SM (d18:1/18:1)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
45	*757,6*	SM (d18:1/20:1)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
46	*759,6*	SM (d18:1/20:0)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
47	*785,591*	SM (d18:1/22:1)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
48	*787,6*	SM (d18:1/22:0)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
49	*799,6*	SM (d18:1/23:1)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
50	*801,6*	SM (d18:1/23:0)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
51	*813,7*	SM (d18:1/24:1)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
52	*827,7*	SM (d18:1/25:1)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
53	*829,7*	SM (d18:1/25:0)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
54	*841,7*	SM (d18:1/26:1)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
55	*843,7*	SM (d18:1/26:0)	*SM (d18:1/12:0)*	*183.9758 - 184.0758*
56	*726,58*	HexCer (d18:1/18:1)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26702*
57	*754,7*	HexCer (d18:1/20:1)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26703*
58	*756,7*	HexCer (d18:1/20:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26704*
59	*782,7*	HexCer (d18:1/22:1)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26705*
60	*784,66*	HexCer (d18:1/22:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26706*
61	*796,7*	HexCer (d18:1/23:1)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26707*
62	*798,7*	HexCer (d18:1/23:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26708*
63	*808,6*	HexCer (d18:1/24:2)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26709*
64	*812,7*	HexCer (d18:1/24:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26710*
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66	*826,8*	HexCer (d18:1/25:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26712*
67	*836,6*	HexCer (d18:1/26:2)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26713*
68	*838,8*	HexCer (d18:1/26:1)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26714*
69	*840,8*	HexCer (d18:1/26:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26715*
70	*716,7*	HexCer OH (d18:1/16:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26716*
71	*744,7*	HexCer OH (d18:1/18:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26717*

72	772,7	HexCer OH (d18:1/20:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26718*
73	798,7	HexCer OH (d18:1/22:1)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26719*
74	800,7	HexCer OH (d18:1/22:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26720*
75	812,7	HexCer OH (d18:1/23:1)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26721*
76	814,7	HexCer OH (d18:1/23:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26722*
77	826,8	HexCer OH (d18:1/24:1)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26723*
78	828,8	HexCer OH (d18:1/24:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26724*
79	840,8	HexCer OH (d18:1/25:1)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26725*
80	842,8	HexCer OH (d18:1/25:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26726*
81	854,8	HexCer OH (d18:1/26:1)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26727*
82	856,8	HexCer OH (d18:1/26:0)	*GlcCer (d18:1/12:0)*	*264.2652 - 264.26728*
83	974,7502	LacCer (d18:0/24:1)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2727*
84	972,7346	LacCer (d18:1/24:1(15Z)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2728*
85	1002,7815	LacCer (d18:0/26:1)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2729*
86	1000,7659	LacCer (d18:1/26:1(17Z))	*LacCer (d18:1/12:0)*	*264.2687 - 264.2730*
87	886,6407	LacCer (d18:1/18:1(9Z))	*LacCer (d18:1/12:0)*	*264.2687 - 264.2731*
88	889,6563	LacCer (d18:0/18:1)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2732*
89	948,7346	LacCer (d18:0/22:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2733*
90	946,7189	LacCer (d18:1/22:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2734*
91	920,7033	LacCer (d18:0/20:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2735*
92	918,6876	LacCer (d18:1/20:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2736*
93	1004,7972	LacCer (d18:0/26:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2737*
94	1002,7815	LacCer(d18:1/26:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2738*
95	864,6407	LacCer (d18:0/16:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2739*
96	806,5624	LacCer (d14:1/16:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2740*
97	892,672	LacCer (d18:0/18:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2741*
98	836,6094	LacCer (d14:0/18:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2742*
99	890,6563	LacCer (d18:1/18:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2743*
100	976,7659	LacCer (d18:0/24:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2744*
101	974,7502	LacCer (d18:1/24:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2745*
102	836,6094	LacCer (d18:0/14:0)	*LacCer (d18:1/12:0)*	*264.2687 - 264.2746*
103	834,5937	LacCer (d18:1/14:0)	*LacCer (d18:1/12:0)*	*264.2687 -264.2747*
104	484,465	dHCer (d18:0/12:0)	*Ceramide (d18:1/12:0)*	*264.2687 -264.2747*
105	540,535	dHCer (d18:0/16:0)	*Ceramide (d18:1/12:0)*	*284.2943 - 284.2983*
106	568,563	dHCer (d18:0/18:0)	*Ceramide (d18:1/12:0)*	*284.2943 - 284.2983*
107	596,5976	dHCer (d18:0/20:0)	*Ceramide (d18:1/12:0)*	*284.2943 - 284.2983*
108	624,6289	dHCer (d18:0/22:0)	*Ceramide (d18:1/12:0)*	*284.2943 - 284.2983*

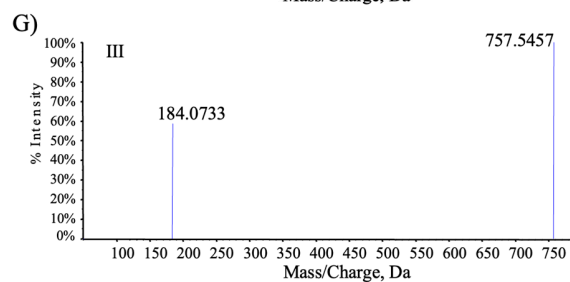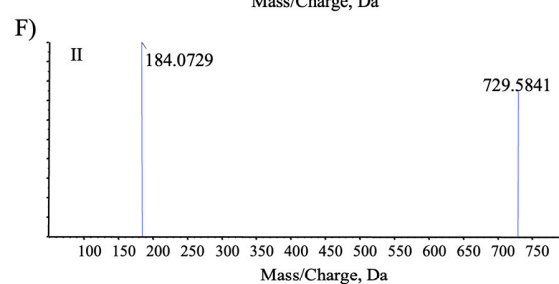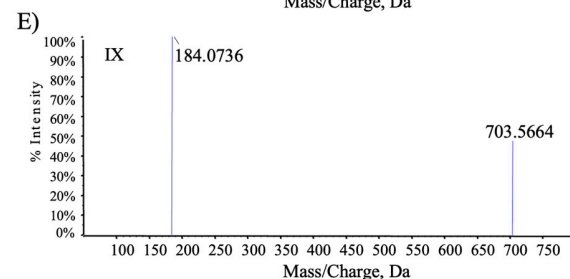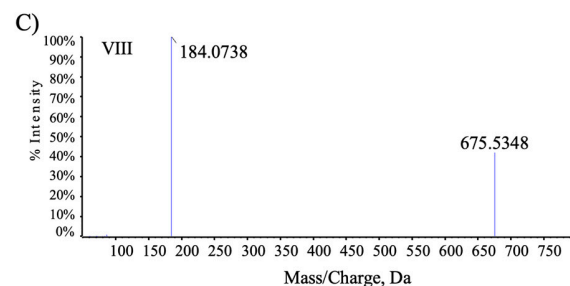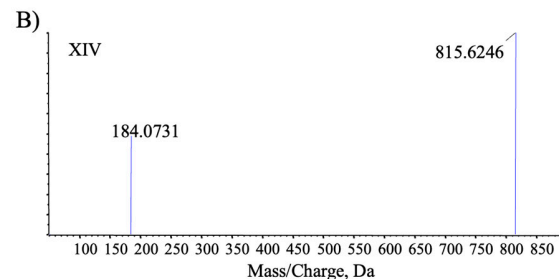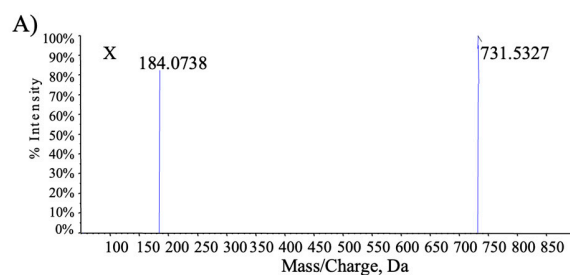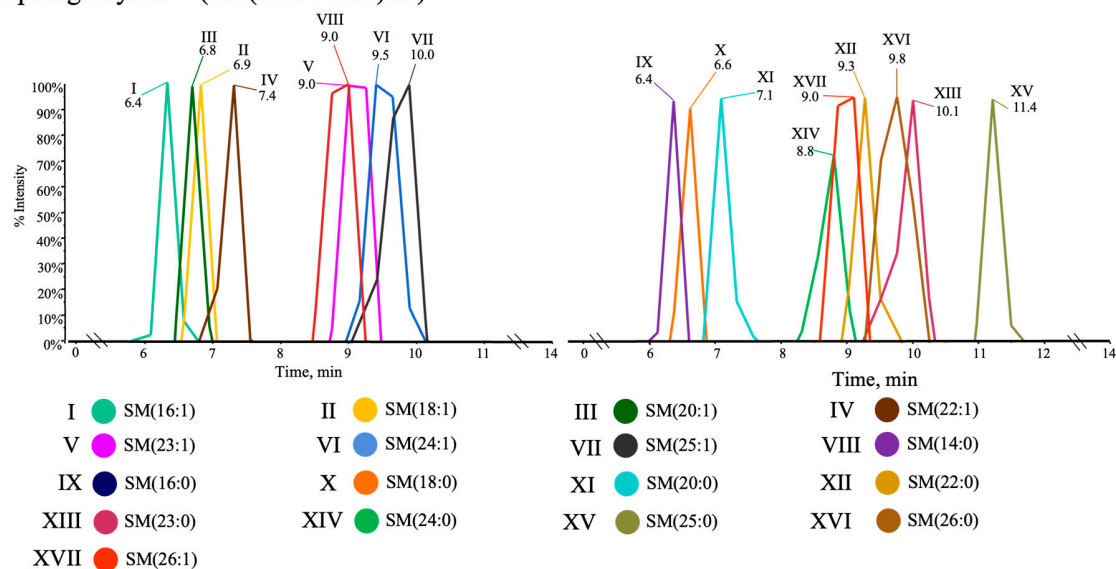| 109	650,6446	dHCer (d18:0/24:1(15Z))	Ceramide (d18:1/12:0)	284.2943 - 284.2983
110	652,6602	dHCer (d18:0/24:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2983
111	678,6759	dHCer (d18:0/26:1(17Z))	Ceramide (d18:1/12:0)	284.2943 - 284.2983
112	680,6915	dHCer (d18:0/26:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2983
113	566,5507	dHCer (d18:0/18:1)	Ceramide (d18:1/12:0)	284.2943 - 284.2983
114	512,5037	dHCer (d18:0/14:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2983
115	668,6551	dHCer (d18:0/h24:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2983
116	696,6864	dHCer (d18:0/h26:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2983
117	570,5456	dHCer (d18:0/h17:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2983
118	498,4881	dHCer (d18:0/13:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2983
119	526,5194	dHCer (d18:0/15:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2983
120	554,5507	dHCer (d18:0/17:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2983
121	568,3566	dHCer (d20:0/16:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2983
122	596,5976	dHCer (d20:0/18:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2983
123	624,6289	dHCer (d20:0/20:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2984
124	652,6602	dHCer (d20:0/22:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2985
125	680,6915	dHCer (d20:0/24:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2986
126	708,7228	dHCer (d20:0/26:0)	Ceramide (d18:1/12:0)	284.2943 - 284.2987

Internal standards (IS)

Supplementary Figure S6. Chromatographic profile and mass spectral data of internal standards used as reference for analysis. (I) Sphingomyelin (d18:0/12:0). (II) Sphingosine (17:0). (III) Sphinganine (17:0). (IV) Ceramide (12:0). (V) Galactosylceramide (12:0). (VI) Ceramide (17:0).
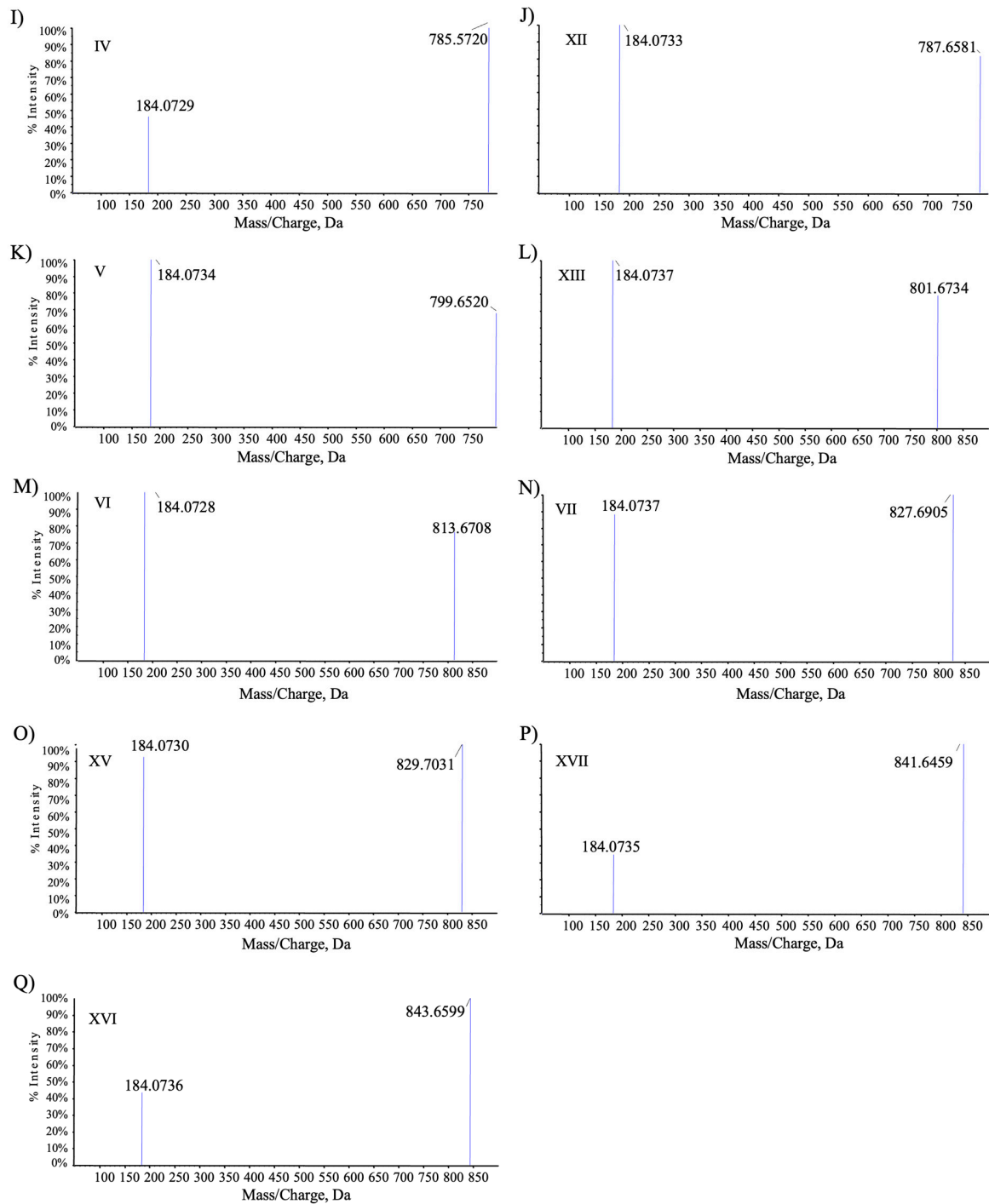
Supplementary Figure S7. Chromatographic profile and mass spectral data of detected ceramides. (I) Ceramide (16:0). (II) Ceramide (18:0). (III) Ceramide (20:0). (IV) Ceramide (22:0). (V) Ceramide (23:0). (VI) Ceramide (24:0). (VII) Ceramide (25:0). (VIII) Ceramide (24:1). (IX) Ceramide (18:1).
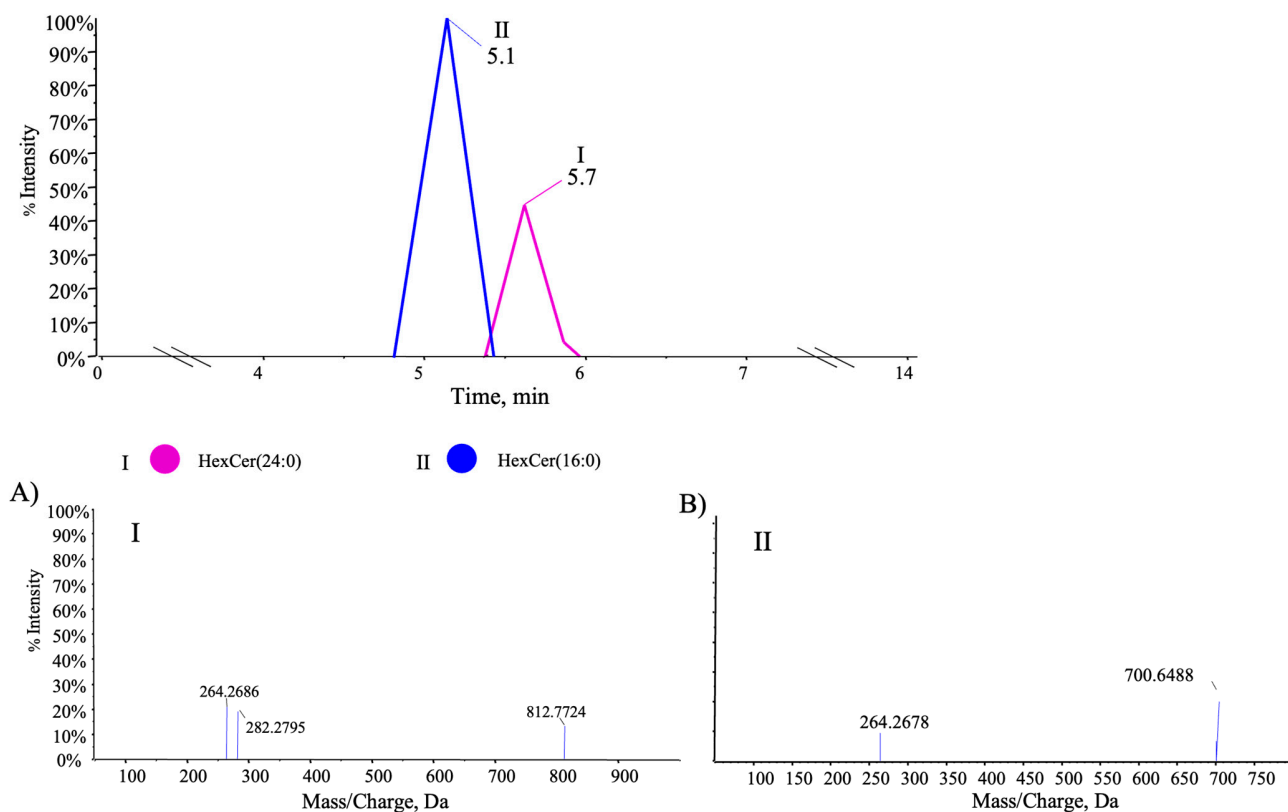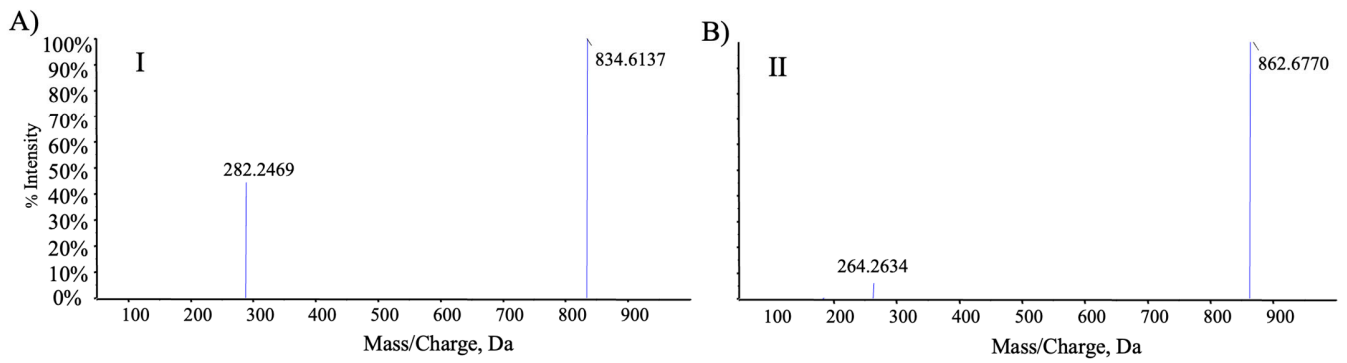
Sphingomyelin – (SM(d18:1/12:0) IS)

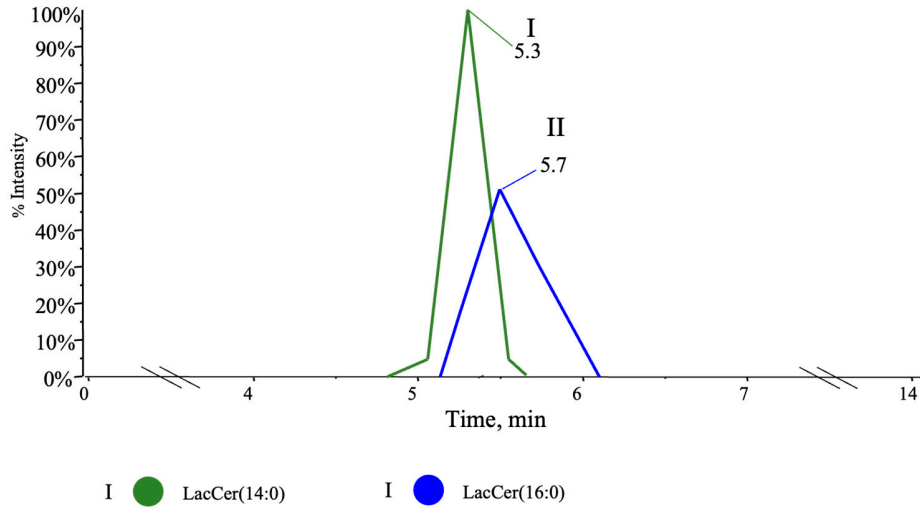|							
I	🟢 SM(16:1)	II	🟡 SM(18:1)	III	🟢 SM(20:1)	IV	🟤 SM(22:1)
V	🟣 SM(23:1)	VI	🔵 SM(24:1)	VII	⚫ SM(25:1)	VIII	🟣 SM(14:0)
IX	🔵 SM(16:0)	X	🟠 SM(18:0)	XI	🔵 SM(20:0)	XII	🟡 SM(22:0)
XIII	🔴 SM(23:0)	XIV	🟢 SM(24:0)	XV	🟢 SM(25:0)	XVI	🟤 SM(26:0)
XVII	🔴 SM(26:1)						

Supplementary Figure S8. Chromatographic profile and mass spectral data of detected sphingomyelins. (I) Sphingomyelin (16:1). (II) Sphingomyelin (18:1). (III) Sphingomyelin (20:1). (IV) Sphingomyelin (22:1). (V) Sphingomyelin (23:1). (VI) Sphingomyelin (24:1). (VII) Sphingomyelin (25:1). (VIII) Sphingomyelin (14:0). (IX) Sphingomyelin (16:0). (X) Sphingomyelin (18:0). (XI) Sphingomyelin (20:0). (XII) Sphingomyelin (22:0). (XIII) Sphingomyelin (23:0). (XIV) Sphingomyelin (24:0). (XV) Sphingomyelin (25:0). (XVI) Sphingomyelin (26:0). (XVII) Sphingomyelin (26:1).
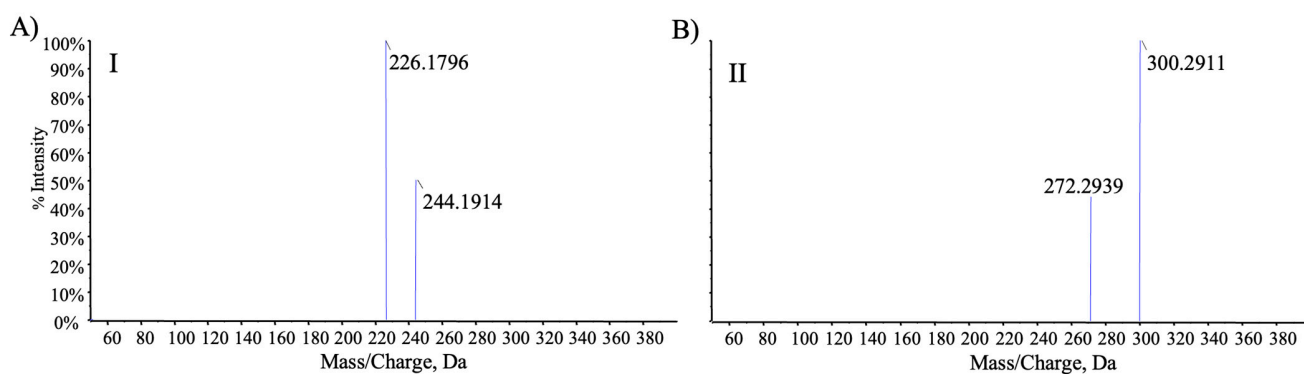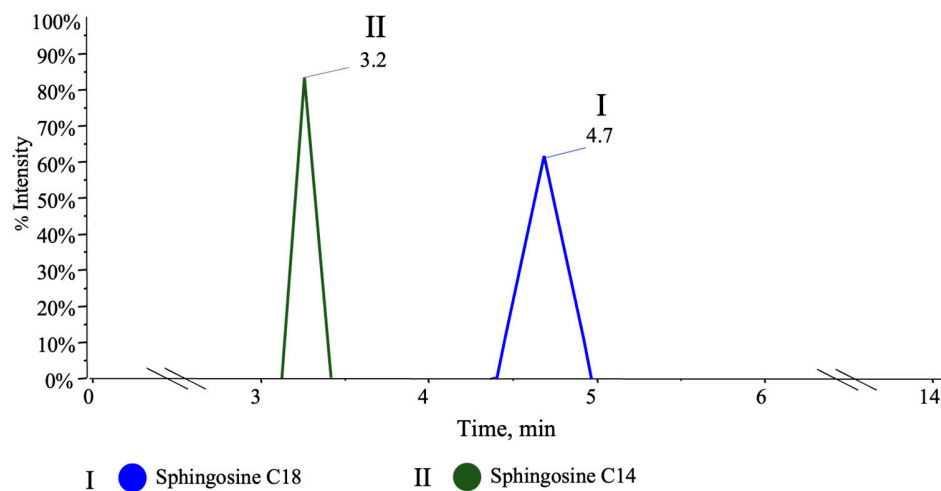
Hexosylceramides - Cer(12:0) IS

Supplementary Figure S9. Chromatographic profile and mass spectral data of detected hexosylceramides. (I) HexosylCeramide (24:0). (II) HexosylCeramide (16:0).

LacCeramides - LacCer(12:0) IS

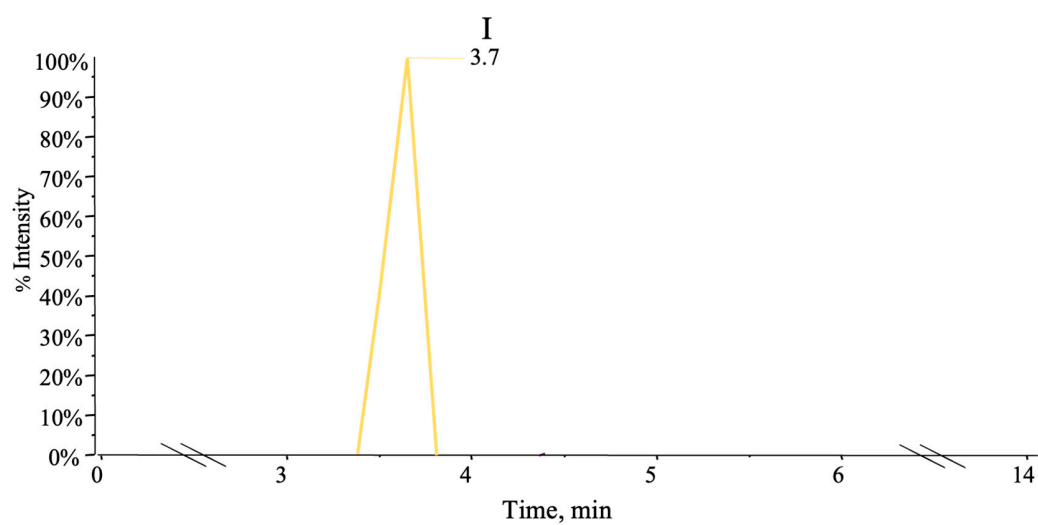I ● LacCer(14:0)   I ● LacCer(16:0)

A)

B)

Supplementary Figure S10. Chromatographic profile and mass spectral data of detected lactosylceramides. (I) LacCer (14:0). (II) LacCer (16:0).
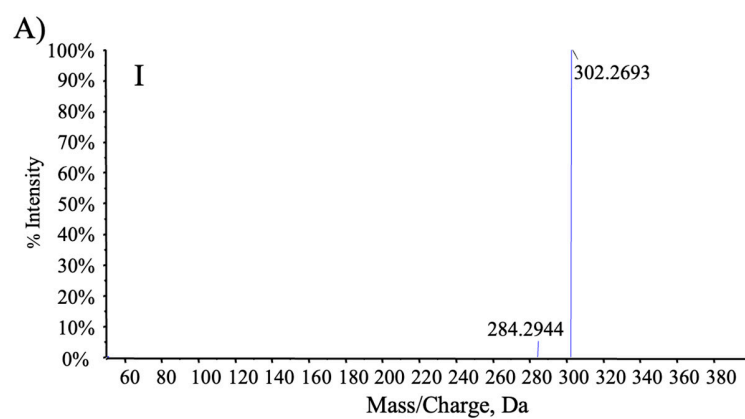
Sphingosine - (Sphingosine C17:0 IS)

Supplementary Figure S11. Chromatographic profile and mass spectral data of detected sphingosines. (I) Sphingosine (18:0). (II) Sphingosine (14:0).
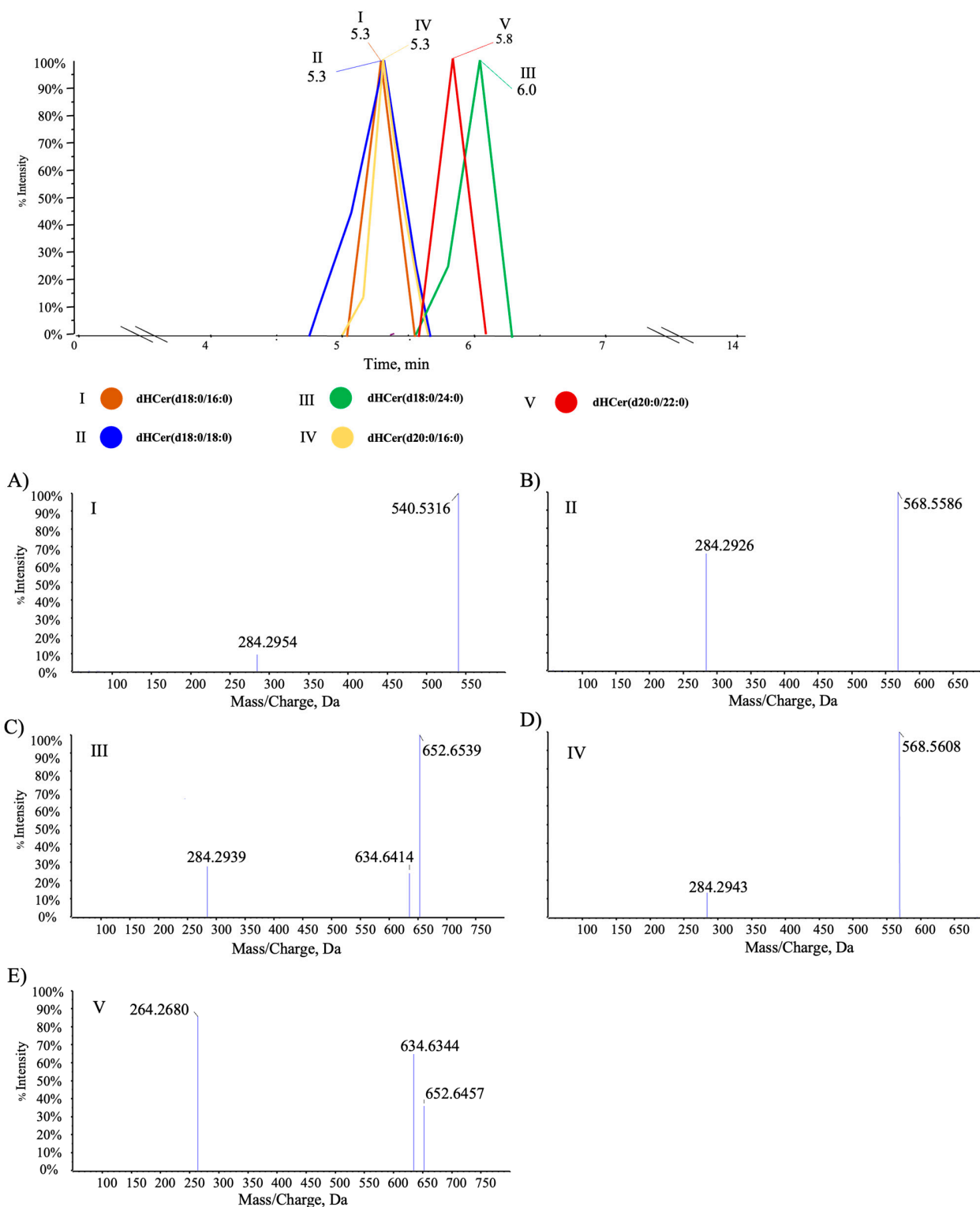
Sphinganine – (Sphingosine C17:0 IS)

Supplementary Figure S12. Chromatographic profile and mass spectral data of detected sphinganines. (I) Sphinganine (18:0).

Supplementary Figure S13. Chromatographic profile and mass spectral data of detected dihydroceramides. (I) dHCer(d18:0/16:0). (II) dHCer(d18:0/18:0). (III) dHCer(d18:0/24:0). (IV) dHCer(d20:0/16:0). (V) dHCer(d20:0/22:0).

Supplementary Table S3. List of sphingolipid pathway enzymes and their respective acronyms and ID number.

Enzyme name	Acronym enzyme	Acronym Gene	HGNC ID	NCBI ID
Serine palmitoyltransferase long chain base subunit 1	SPT	SPTLC1	11277	10558
Serine palmitoyltransferase long chain base subunit 2	SPT	SPTLC2	11278	9517
Serine palmitoyltransferase long chain base subunit 3	SPT	SPTLC3	16253	55304
3-ketodihydrosphingosine reductase	KDR	KDSR	4021	2531
Ceramide synthase 1	CerS	CERS1	14253	10715
Ceramide synthase 2	CerS	CERS2	14076	29956
Ceramide synthase 3	CerS	CERS3	23752	204219
Ceramide synthase 4	CerS	CERS4	23747	79603
Ceramide synthase 5	CerS	CERS5	23749	91012
Ceramide synthase 6	CerS	CERS6	23826	253782
Sphingomyelin synthase 1	SMS	SGMS1	29799	259230
Sphingomyelin synthase 2	SMS	SGMS2	28395	166929
Sphingomyelin phosphodiesterase 1	SMase	SMPD1	11120	6609
Sphingomyelin phosphodiesterase 2	SMase	SMPD2	11121	6610
Sphingomyelin phosphodiesterase 3	SMase	SMPD3	14240	55512
Sphingomyelin phosphodiesterase 4	SMase	SMPD4	32949	55627
N-acylsphingosine amidohydrolase (acid ceramidase)	Csase	ASAH1	735	427
N-acylsphingosine amidohydrolase 2 (Neutral ceramidase/non-lysosomal ceramidase)	Csase	ASAH2	18860	56624
Ceramide synthase 1	CerS	CERS1	14253	10715
Ceramide synthase 2	CerS	CERS2	14076	29956
Ceramide synthase 3	CerS	CERS3	23752	204219
Ceramide synthase 4	CerS	CERS4	23747	79603
Ceramide synthase 5	CerS	CERS5	23749	91012
Ceramide synthase 6	CerS	CERS6	23826	253782