Supplementary information

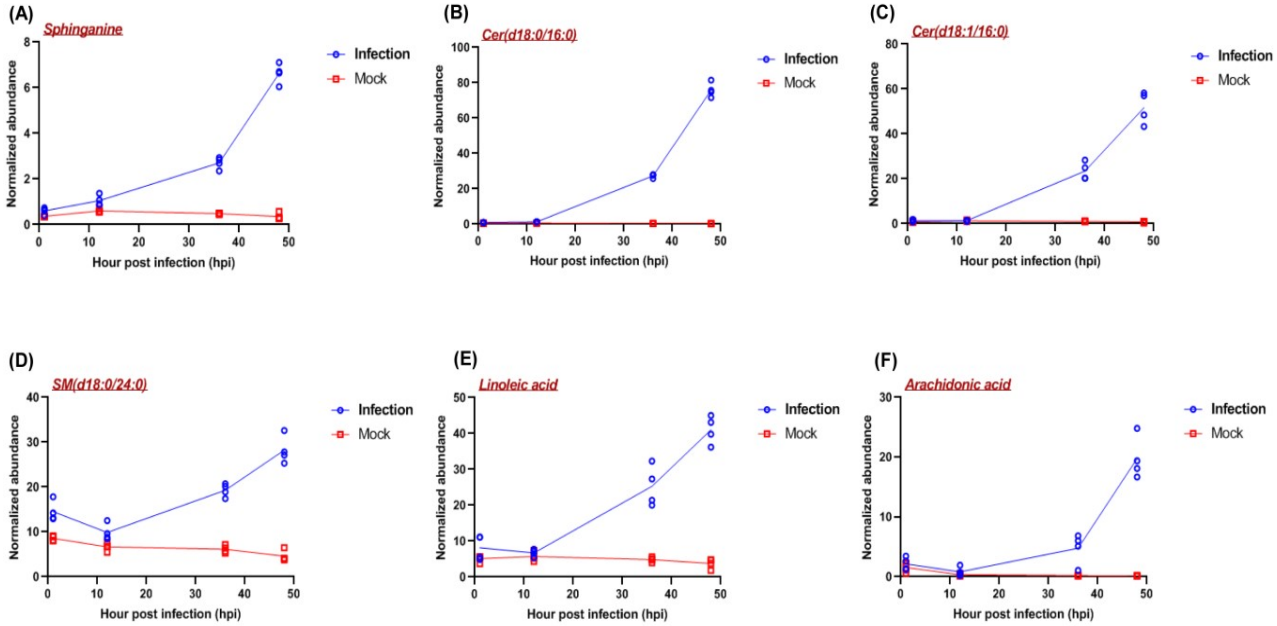

Figure S1. (A-F) The abundance trend of selected representative lipids at different infection time points. Data are shown as an individual measurement of four independent experiments (n=4) for infected and mock samples respectively at each time point. **(A)** Sphinganine, **(B)** Cer(d18:0/16:0), **(C)** Cer(d18:1/16:0), **(D)** SM(d18:0/24:0), **(E)** Linoleic acid, **(F)** Arachidonic acid.

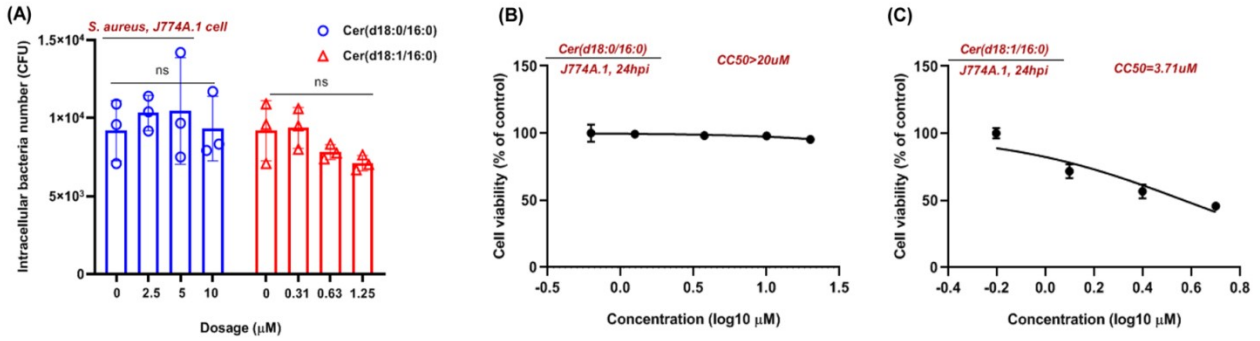

Figure S2. (A) Intracellular bacterial loads were determined by counting CFU after different concentration of cer(d18:0/16:0) and cer(d18:1/16:0) treatments. **(B and C)** *In vitro* cytotoxicity assays of cer(d18:0/16:0) **(B)** and cer(d18:1/16:0) **(C)** were shown. Cells were incubated with different dosage of cer(d18:0/16:0) and cer(d18:1/16:0) or DMSO for 24 hours to evaluate cytotoxicity by MTT assay.

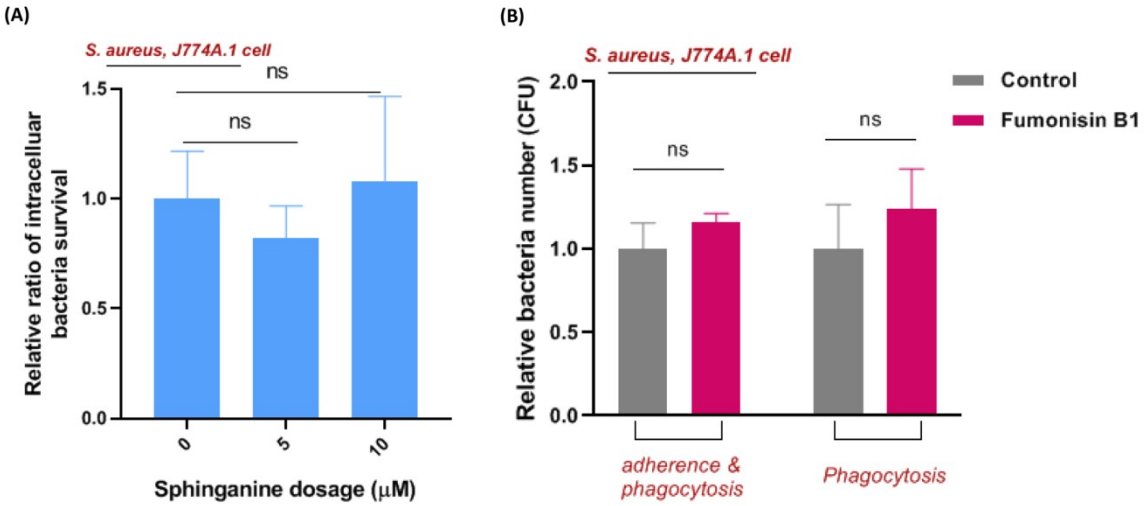

Figure S3. (A) The relative ratios of intracellular survival of *S. aureus* after sphinganine treatment for 24 hours. **(B)** The relative bacterial number comparison of *S. aureus* adhesion and phagocytosis by J774A.1 cells after fumonisin treatment for 1 and 2 hours respectively. The numbers of bacterial CFU released from the lysed macrophages were determined by plating lysates on BHI agar plates.

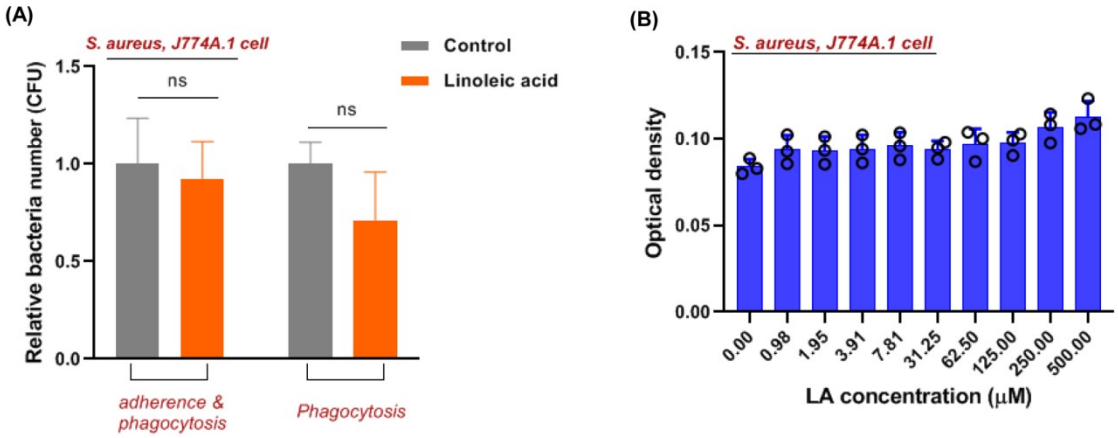

Figure S4. (A) The relative bacterial number comparison of *S. aureus* adhesion and phagocytosis by J774A.1 cells after linoleic acid treatment for 1 and 2 hours respectively. The numbers of bacterial CFU released from the lysed macrophages were determined by plating lysates on BHI agar plates. **(B)** The minimum inhibitory concentration measurement of linoleic acid (LA) incubated with *S. aureus* in Dulbecco's Modified Eagle Medium (DMEM) for 18 hours.

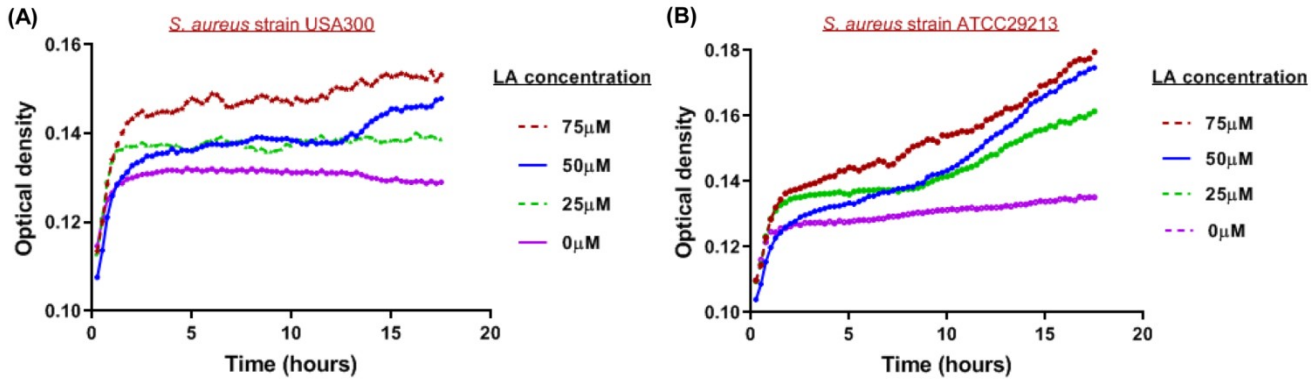

Figure S5. (A and B) The dynamic growth curve of *S. aureus* USA 300 strain **(A)** and ATCC29213 **(B)** treated with different concentrations of linoleic acid (LA) for 18 hours in Dulbecco's Modified Eagle Medium (DMEM).

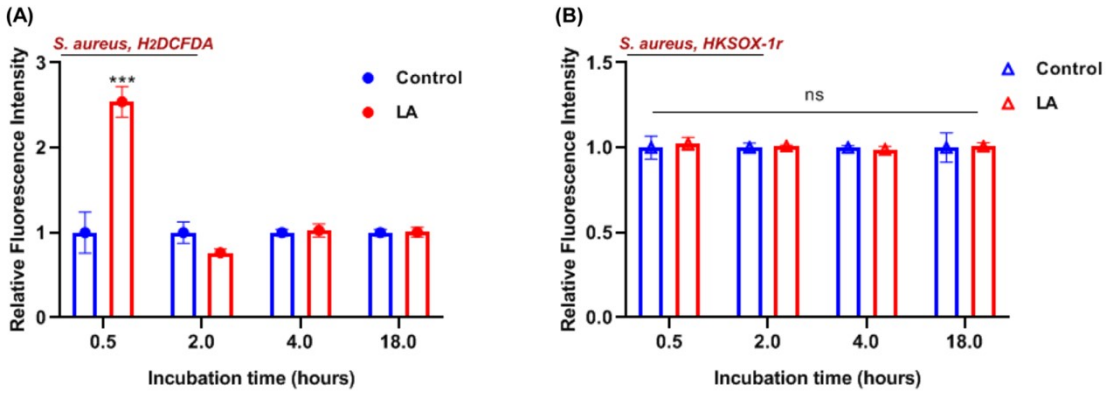

Figure S6. (A and B) Quantified relative fluorescence intensities of ROS (H2DCFDA probe, **A**) and superoxide (HKSOX-1r probe, **B**) upon LA (25 µM) treatments at indicated incubation times in *S. aureus*. Data are shown as mean ± SD of four independent experiments. Unpaired t-test was used to analyze the significance of the observed differences. For all statistical analysis above, *p<0.05, **p<0.01 and ***p<0.001.

Table S1. The coefficient of variation (CV) of spike-in standards in the current analytical batch

Lipids name	Retention time (min)	Accurate mass	Detection mode	Adduct ion name	CV in 1h samples	CV in 12h samples	CV in 36h samples	CV in 48h samples	CV in QC samples
Arachidonic acid-d8	2.02	311.2829	negative	$[M-H]^-$	12.54%	14.22%	12.36%	14.67%	5.18%
15(s)-HETE-d8	1.04	327.2768	negative	$[M-H]^-$	6.67%	10.17%	4.66%	5.23%	3.82%
Leukotriene-B4-d4	0.82	339.2483	negative	$[M-H]^-$	9.59%	17.78%	18.56%	17.58%	9.90%
PAF-C16-d4	1.66	528.3975	positive	$[M+H]^+$	7.33%	8.38%	9.84%	2.86%	17.50%

Table S2. The 158 lipids that were significantly different between bacterial infections and mock controls

Time point	Lipids id	Significant lipids	Detection mode	Retention time	Accurate mass	Adduct ion name	Lipids species	Identification information	Fold change in infected vs control	p-Value in infected vs control	VIP in infected vs control
1hr	477	PE(16:0/0:0)	Neg	1.40	452.2773	[M-H]-	LPE	MS/MS	2.04	0.0474	1.03
1hr	542	PE(18:0/0:0)	Neg	1.92	480.3093	[M-H]-	LPE	MS/MS	2.12	0.0472	1.02
1hr	682	PC(O-16:0/0:0)	Pos	1.55	482.3623	[M+H]+	EtherLPC	MS/MS	2.14	0.0337	2.82
12hr	1360	PC(16:1/16:1)	Pos	4.92	730.5399	[M+H]+	PC	MS/MS	0.50	0.0118	4.45
12hr	512	PE(O-18:0/0:0)	Neg	2.27	466.3282	[M-H]-	EtherLPE	MS/MS	2.62	0.0005	1.15
12hr	1014	PG(15:0/15:0)	Neg	4.82	693.4702	[M-H]-	PG	MS/MS	2.33	0.0090	0.99
12hr	249	Sphinganine	Pos	1.35	302.3061	[M+H]+	SPB	STD	2.04	0.0001	0.54
12hr	1046	Cer(d18:0/22:0)	Pos	13.91	624.6259	[M+H]+	Cer	MS/MS	4.72	0.0000	1.77
12hr	1117	Cer(d18:0/24:0)	Pos	14.38	652.6591	[M+H]+	Cer	MS/MS	7.29	0.0005	1.89
12hr	1107	Cer(d18:0/24:1)	Pos	13.89	650.6447	[M+H]+	Cer	MS/MS	5.26	0.0001	1.65
12hr	1564	GlcCer(d18:0/22:0)	Pos	13.42	786.6767	[M+H]+	Cer	MS/MS	2.54	0.0008	0.99
12hr	1072	Cer(d18:0/23:0)	Pos	14.15	638.6437	[M+H]+	Cer	MS/MS	2.83	0.0000	0.63
36hr	199	Arachidonic acid	Neg	2.08	303.229	[M-H]-	FFA	STD	31.72	0.0118	0.79
36hr	142	Linoleic acid	Neg	2.22	279.2329	[M-H]-	FFA	STD	4.90	0.0153	1.45
36hr	271	Docosapentaenoic acid	Neg	2.15	329.2465	[M-H]-	FFA	STD	14.69	0.0149	1.14
36hr	147	Oleic acid	Neg	2.87	281.2485	[M-H]-	FFA	STD	4.05	0.0039	1.63
36hr	249	Sphinganine	Pos	1.35	302.3061	[M+H]+	SPB	STD	5.61	0.0000	0.62
36hr	1660	SM(d18:0/24:1)	Pos	13.20	815.6995	[M+H]+	SM	MS/MS	2.24	0.0000	2.46
36hr	1576	SM(d18:0/22:0)	Pos	13.22	789.6842	[M+H]+	SM	MS/MS	2.49	0.0000	1.74
36hr	1669	SM(d18:0/24:0)	Pos	13.79	817.7166	[M+H]+	SM	MS/MS	3.15	0.0000	1.51
36hr	1175	SM(d18:1/14:0)	Pos	4.53	675.545	[M+H]+	SM	MS/MS	0.28	0.0000	2.50
36hr	1557	SM(d18:1/22:1)	Pos	10.26	785.6556	[M+H]+	SM	MS/MS	0.45	0.0001	1.47
36hr	1734	SM(d18:1/26:1)	Pos	13.55	841.7136	[M+H]+	SM	MS/MS	0.39	0.0000	0.80
36hr	831	Cer(d18:0/16:0)	Pos	9.06	540.5351	[M+H]+	Cer	MS/MS	69.80	0.0000	2.17
36hr	973	Cer(d18:0/20:0)	Pos	13.37	596.5977	[M+H]+	Cer	MS/MS	15.77	0.0000	0.91

36hr	1046	Cer(d18:0/22:0)	Pos	13.91	624.6259	[M+H]+	Cer	MS/MS	50.14	0.0000	2.51
36hr	1037-p	Cer(d18:0/22:1)	Pos	13.35	622.6116	[M+H]+	Cer	MS/MS	40.99	0.0000	0.96
36hr	1066	Cer(d18:0/23:1)	Pos	13.98	636.6281	[M+H]+	Cer	MS/MS	12.11	0.0000	0.89
36hr	889	Cer(d18:0/24:0)	Neg	14.42	650.6456	[M-H]-	Cer	MS/MS	32.41	0.0000	0.78
36hr	828	Cer(d18:1/16:0)	Pos	8.22	538.5209	[M+H]+	Cer	MS/MS	22.60	0.0000	1.95
36hr	1038-p	Cer(d18:1/22:0)	Pos	13.73	622.6124	[M+H]+	Cer	MS/MS	19.84	0.0000	1.97
36hr	1035	Cer(d18:1/22:1)	Pos	13.14	620.5943	[M+H]+	Cer	MS/MS	12.05	0.0000	1.04
36hr	1061	Cer(d18:1/23:1)	Pos	13.44	634.6111	[M+H]+	Cer	MS/MS	16.17	0.0000	0.90
36hr	1108	Cer(d18:1/24:0)	Pos	14.23	650.6452	[M+H]+	Cer	MS/MS	7.11	0.0000	2.49
36hr	1102	Cer(d18:1/24:1)	Pos	13.71	648.6284	[M+H]+	Cer	MS/MS	13.15	0.0000	3.05
36hr	1564	GlcCer(d18:0/22:0)	Pos	13.42	786.6767	[M+H]+	Cer	MS/MS	10.74	0.0000	0.68
36hr	1072	GlcCer(d18:0/23:0)	Pos	14.15	638.6437	[M+H]+	Cer	MS/MS	26.78	0.0000	0.84
36hr	2034	CL(1'-[16:0/18:1],3'-[16:0/18:1])	Neg	15.33	1403.9961	[M-H]-	CL	MS/MS	2.37	0.0000	1.29
36hr	1017	DG(16:0/18:1/0:0)	Pos	13.02	612.5557	[M+NH4]+	DG	MS/MS	0.44	0.0000	1.16
36hr	1287	PC(14:0/16:0)	Neg	6.62	764.5466	[M+Hac-H]-	PC	MS/MS	5.30	0.0001	1.63
36hr	1186	PC(14:0/14:0)	Pos	4.59	678.5083	[M+H]+	PC	MS/MS	0.28	0.0000	4.47
36hr	1267	PC(14:0/16:1)	Pos	4.77	704.5242	[M+H]+	PC	MS/MS	0.31	0.0000	4.17
36hr	1323	PC(15:0/16:0)	Pos	6.53	720.5542	[M+H]+	PC	MS/MS	6.26	0.0000	3.27
36hr	1359	PC(32:2)	Pos	5.74	730.5393	[M+H]+	PC	MS/MS	2.69	0.0014	0.84
36hr	1360	PC(16:1/16:1)	Pos	4.92	730.5399	[M+H]+	PC	MS/MS	0.19	0.0000	5.00
36hr	1421	PC(16:0/17:0)	Pos	8.56	748.5853	[M+H]+	PC	MS/MS	2.33	0.0000	1.48
36hr	1412	PC(15:0/18:1)	Pos	6.74	746.5699	[M+H]+	PC	MS/MS	3.02	0.0002	1.61
36hr	1538	PC(16:0/20:4)	Pos	6.30	782.5695	[M+H]+	PC	MS/MS	6.94	0.0000	2.99
36hr	1531	PC(16:0/20:5)	Pos	5.28	780.555	[M+H]+	PC	MS/MS	6.30	0.0001	1.14
36hr	1625	PC(16:0/22:6)	Pos	5.81	806.5711	[M+H]+	PC	MS/MS	8.20	0.0001	2.72
36hr	1719	PC(18:0/22:5)	Pos	8.37	836.6152	[M+H]+	PC	MS/MS	15.17	0.0000	1.11
36hr	1713	PC(18:0/22:6)	Pos	7.69	834.5999	[M+H]+	PC	MS/MS	15.41	0.0000	1.26
36hr	1770	PC(18:1/24:1)	Pos	13.59	870.6934	[M+H]+	PC	MS/MS	3.64	0.0001	1.13
36hr	713	PC(16:0/0:0)	Pos	1.33	496.3409	[M+H]+	LPC	MS/MS	0.48	0.0002	1.66
36hr	1467	PC(O-14:0/21:1)	Pos	10.97	760.6216	[M+H]+	Ether-PC	MS/MS	2.43	0.0001	0.90

36hr	1517	PC(O-14:0/22:1)	Pos	12.86	774.6379	[M+H]+	Ether-PC	MS/MS	2.08	0.0000	1.59
36hr	1278	PC(O-31:0)	Pos	7.69	706.5745	[M+H]+	Ether-PC	MS/MS	2.40	0.0000	1.11
36hr	1503-p	PC(O-36:3)	Pos	8.31	770.6057	[M+H]+	Ether-PC	MS/MS	4.95	0.0000	1.37
36hr	1484	PC(O-18:0/18:5)	Pos	6.15	766.5747	[M+H]+	Ether-PC	MS/MS	10.73	0.0000	1.47
36hr	1613	PC(O-14:0/24:2)	Pos	12.92	800.6533	[M+H]+	Ether-PC	MS/MS	2.34	0.0002	1.19
36hr	1598	PC(O-14:0/24:4)	Pos	9.76	796.6219	[M+H]+	Ether-PC	MS/MS	5.45	0.0001	0.87
36hr	1589	PC(O-16:0/22:5)	Pos	7.50	794.6072	[M+H]+	Ether-PC	MS/MS	6.70	0.0001	2.46
36hr	1583	PC(O-16:0/22:6)	Pos	6.84	792.5917	[M+H]+	Ether-PC	MS/MS	9.01	0.0000	2.41
36hr	993	PE(16:1/16:1)	Neg	5.31	686.4756	[M-H]-	PE	MS/MS	0.34	0.0005	0.72
36hr	1312	PE(18:0/20:1)	Neg	10.78	772.5868	[M-H]-	PE	MS/MS	2.07	0.0000	0.70
36hr	454	PE(O-16:0/0:0)	Neg	1.61	438.2962	[M-H]-	Ether-LPE	MS/MS	3.37	0.0003	0.89
36hr	512	PE(O-18:0/0:0)	Neg	2.27	466.3282	[M-H]-	Ether-LPE	MS/MS	4.85	0.0002	0.67
36hr	1435	PE(O-38:5)	Pos	8.08	752.5586	[M+H]+	Ether-PE	MS/MS	19.78	0.0000	1.08
36hr	1050	PE(O-16:0/18:1)	Neg	10.54	702.5435	[M-H]-	Ether-PE	MS/MS	7.90	0.0001	1.34
36hr	1143	PE(O-36:1)	Neg	12.99	730.5742	[M-H]-	Ether-PE	MS/MS	3.11	0.0004	1.43
36hr	1118	PE(O-36:4)	Neg	8.10	724.5287	[M-H]-	Ether-PE	MS/MS	18.92	0.0000	2.71
36hr	1240	PE(O-18:0/20:4)	Neg	10.77	752.5615	[M-H]-	Ether-PE	MS/MS	4.87	0.0001	2.39
36hr	1347	PE(O-18:0/22:5)	Neg	10.79	778.587	[M-H]-	Ether-PE	MS/MS	5.72	0.0001	1.73
36hr	1231	PE(P-18:0/20:4)	Neg	10.23	750.5458	[M-H]-	Ether-PE	MS/MS	2.13	0.0048	1.16
36hr	1325	PE(P-18:0/22:6)	Neg	9.46	774.55	[M-H]-	Ether-PE	MS/MS	2.24	0.0030	1.00
36hr	614	PG(18:0/0:0)	Neg	1.49	511.3034	[M-H]-	LPG	MS/MS	32.73	0.0001	0.76
36hr	1099	PG(14:0/18:1)	Neg	4.18	719.4863	[M-H]-	PG	MS/MS	0.47	0.0061	0.77
36hr	1503	PG(18:2/22:6)	Neg	3.59	817.5042	[M-H]-	PG	MS/MS	2.20	0.0055	0.63
36hr	1556	PI(16:1/18:1)	Neg	4.77	833.5212	[M-H]-	PI	MS/MS	0.15	0.0000	1.99
36hr	1645	PI(18:1/18:1)	Neg	6.10	861.5536	[M-H]-	PI	MS/MS	0.42	0.0002	3.76
36hr	1708	PI(18:1/20:3)	Neg	6.14	885.5534	[M-H]-	PI	MS/MS	2.88	0.0008	2.12
36hr	1703	PI(18:1/20:4)	Neg	4.89	883.5369	[M-H]-	PI	MS/MS	2.19	0.0054	1.28
36hr	1153	PS(16:0/16:1)	Neg	4.85	732.4832	[M-H]-	PS	MS/MS	0.43	0.0005	1.19
48hr	199	Arachidonic acid	Neg	2.08	303.229	[M-H]-	FFA	STD	139.10	0.0000	1.18
48hr	142	Linoleic acid	Neg	2.22	279.2329	[M-H]-	FFA	STD	10.83	0.0004	1.53
48hr	147	Oleic acid	Neg	2.87	281.2485	[M-H]-	FFA	STD	6.40	0.0002	1.63

48hr	249	Sphinganine	Pos	1.35	302.3061	[M+H]+	SPB	STD	18.62	0.0000	0.71
48hr	1275	SM(d18:0/16:0)	Pos	6.50	705.5903	[M+H]+	SM	MS/MS	5.14	0.0000	4.28
48hr	1660	SM(d18:0/24:1)	Pos	13.20	815.6995	[M+H]+	SM	MS/MS	5.42	0.0000	2.65
48hr	1576	SM d18:0/22:0	Pos	13.22	789.6842	[M+H]+	SM	MS/MS	5.79	0.0000	1.77
48hr	1669	SM d18:0/24:0	Pos	13.79	817.7166	[M+H]+	SM	MS/MS	6.15	0.0000	1.37
48hr	1265	SM(d18:1/16:0)	Pos	5.87	703.576	[M+H]+	SM	MS/MS	2.01	0.0000	6.93
48hr	973	Cer(d18:0/20:0)	Pos	13.37	596.5977	[M+H]+	Cer	MS/MS	43.46	0.0000	1.01
48hr	1037-p	Cer(d18:0/22:1)	Pos	13.35	622.6116	[M+H]+	Cer	MS/MS	163.23	0.0000	1.17
48hr	1066	Cer(d18:0/23:1)	Pos	13.98	636.6281	[M+H]+	Cer	MS/MS	34.75	0.0000	0.99
48hr	828	Cer(d18:1/16:0)	Pos	8.22	538.5209	[M+H]+	Cer	MS/MS	62.79	0.0000	2.01
48hr	968	Cer(d18:1/20:0)	Pos	13.14	594.5796	[M+H]+	Cer	MS/MS	39.95	0.0000	1.09
48hr	1038-p	Cer(d18:1/22:0)	Pos	13.73	622.6124	[M+H]+	Cer	MS/MS	56.02	0.0000	2.12
48hr	1061	Cer(d18:1/23:1)	Pos	13.44	634.6111	[M+H]+	Cer	MS/MS	52.94	0.0000	1.01
48hr	1108	Cer(d18:1/24:0)	Pos	14.23	650.6452	[M+H]+	Cer	MS/MS	20.14	0.0000	2.71
48hr	1102	Cer(d18:1/24:1)	Pos	13.71	648.6284	[M+H]+	Cer	MS/MS	47.00	0.0000	3.36
48hr	1072	GlcCer(d18:0/23:0)	Pos	14.15	638.6437	[M+H]+	Cer	MS/MS	59.04	0.0000	0.90
48hr	1658	GlcCer(d18:0/24:0)	Pos	13.92	814.7109	[M+H]+	Cer	MS/MS	33.69	0.0000	0.84
48hr	2034	CL(1'-[16:0/18:1],3'-[16:0/18:1])	Neg	15.33	1403.9961	[M-H]-	CL	MS/MS	5.39	0.0000	1.34
48hr	2030	CL(1'-[16:0/18:1],3'-[16:1/18:1])	Neg	15.10	1401.9806	[M-H]-	CL	MS/MS	2.79	0.0003	1.12
48hr	2057	CL(1'-[16:1/18:0],3'-[18:1/18:1])	Neg	15.33	1430.0106	[M-H]-	CL	MS/MS	3.92	0.0000	1.09
48hr	454	PE(O-16:0/0:0)	Neg	1.61	438.2962	[M-H]-	Ether-LPE	MS/MS	7.84	0.0000	0.95
48hr	512	PE(O-18:0/0:0)	Neg	2.27	466.3282	[M-H]-	Ether-LPE	MS/MS	10.79	0.0000	0.67
48hr	1186	PC(14:0/14:0)	Pos	4.59	678.5083	[M+H]+	PC	MS/MS	0.42	0.0085	2.55
48hr	1287	PC(14:0/16:0)	Neg	6.62	764.5466	[M-H]-	PC	MS/MS	8.21	0.0001	1.36
48hr	1323	PC(15:0/16:0)	Pos	6.53	720.5542	[M+H]+	PC	MS/MS	12.09	0.0000	2.93
48hr	1412	PC(15:0/18:1)	Pos	6.74	746.5699	[M+NH4]+	PC	MS/MS	5.90	0.0001	1.55
48hr	1491	PC(15:0/20:4)	Pos	7.06	768.5585	[M+Na]+	PC	MS/MS	5.65	0.0000	1.04
48hr	1421	PC(16:0/17:0)	Pos	8.56	748.5853	[M+H]+	PC	MS/MS	4.91	0.0000	1.57
48hr	1538	PC(16:0/20:4)	Pos	6.30	782.5695	[M+H]+	PC	MS/MS	22.07	0.0000	3.16
48hr	1531	PC(16:0/20:5)	Pos	5.28	780.555	[M+H]+	PC	MS/MS	17.68	0.0000	1.22
48hr	1625	PC(16:0/22:6)	Pos	5.81	806.5711	[M+H]+	PC	MS/MS	29.52	0.0000	3.01

48hr	1360	PC(16:1/16:1)	Pos	4.92	730.5399	[M+H]+	PC	MS/MS	0.34	0.0055	2.54
48hr	1719	PC(18:0/22:5)	Pos	8.37	836.6152	[M+H]+	PC	MS/MS	55.22	0.0000	1.25
48hr	1713	PC(18:0/22:6)	Pos	7.69	834.5999	[M+H]+	PC	MS/MS	63.30	0.0000	1.55
48hr	1630	PC(18:1/20:4)	Pos	6.39	808.5858	[M+H]+	PC	MS/MS	26.57	0.0000	2.53
48hr	1770	PC(18:1/24:1)	Pos	13.59	870.6934	[M+H]+	PC	MS/MS	5.97	0.0000	1.11
48hr	1359	PC(32:2)	Pos	5.74	730.5393	[M+H]+	PC	MS/MS	8.29	0.0000	1.02
48hr	1312	PE(18:0/20:1)	Neg	10.78	772.5868	[M-H]-	PE	MS/MS	3.11	0.0001	0.68
48hr	1190	PE(18:1/18:1)	Neg	9.06	742.5417	[M-H]-	PE	MS/MS	2.02	0.0041	1.33
48hr	682	PC(O-16:0/0:0)	Pos	1.55	482.3623	[M+H]+	Ether-LPC	MS/MS	2.55	0.0002	1.02
48hr	1368	PC(O-14:0/19:1)	Pos	8.33	732.5909	[M+H]+	Ether-PC	MS/MS	4.61	0.0000	1.99
48hr	1467	PC(O-14:0/21:1)	Pos	10.97	760.6216	[M+H]+	Ether-PC	MS/MS	5.37	0.0000	1.05
48hr	1517	PC(O-14:0/22:1)	Pos	12.86	774.6379	[M+H]+	Ether-PC	MS/MS	4.48	0.0000	1.78
48hr	1613	PC(O-14:0/24:2)	Pos	12.92	800.6533	[M+H]+	Ether-PC	MS/MS	5.41	0.0000	1.42
48hr	1598	PC(O-14:0/24:4)	Pos	9.76	796.6219	[M+H]+	Ether-PC	MS/MS	15.84	0.0000	1.03
48hr	1583	PC(O-16:0/22:6)	Pos	6.84	792.5917	[M+H]+	Ether-PC	MS/MS	23.93	0.0000	2.56
48hr	1484	PC(O-18:0/18:5)	Pos	6.15	766.5747	[M+H]+	Ether-PC	MS/MS	30.02	0.0000	1.58
48hr	1278	PC(O-31:0)	Pos	7.69	706.5745	[M+H]+	Ether-PC	MS/MS	5.92	0.0000	1.35
48hr	1503-p	PC(O-36:3)	Pos	8.31	770.6057	[M+H]+	Ether-PC	MS/MS	12.38	0.0000	1.43
48hr	1252	PE(O-16:0/18:3)	Pos	8.03	700.5284	[M+H]+	Ether-PE	MS/MS	4.65	0.0000	1.14
48hr	1037	PE(P-18:0/16:1)	Neg	10.79	700.5297	[M-H]-	Ether-PE	MS/MS	2.02	0.0002	0.98
48hr	1038	PE(P-16:0/18:1)	Neg	10.09	700.5308	[M-H]-	Ether-PE	MS/MS	2.34	0.0009	2.69
48hr	1050	PE(O-16:0/18:1)	Neg	10.54	702.5435	[M-H]-	Ether-PE	MS/MS	15.20	0.0000	1.29
48hr	1103	PE(O-16:1/20:5)	Neg	6.43	720.4991	[M-H]-	Ether-PE	MS/MS	3.29	0.0002	1.35
48hr	1240	PE(O-18:0/20:4)	Neg	10.77	752.5615	[M-H]-	Ether-PE	MS/MS	8.92	0.0000	2.08
48hr	1347	PE(O-18:0/22:5)	Neg	10.79	778.587	[M-H]-	Ether-PE	MS/MS	9.06	0.0000	1.51
48hr	1344	PE(O-18:1/18:3)	Pos	8.08	726.5424	[M+H]+	Ether-PE	MS/MS	24.06	0.0000	1.14
48hr	1143	PE(O-36:1)	Neg	12.99	730.5742	[M-H]-	Ether-PE	MS/MS	6.49	0.0000	1.48
48hr	1118	PE(O-36:4)	Neg	8.10	724.5287	[M-H]-	Ether-PE	MS/MS	33.21	0.0000	2.19
48hr	1435	PE(O-38:5)	Pos	8.08	752.5586	[M+H]+	Ether-PE	MS/MS	51.70	0.0000	1.08
48hr	1112	PE(P-16:0/20:4)	Neg	7.73	722.5151	[M-H]-	Ether-PE	MS/MS	3.25	0.0000	3.03
48hr	1331	PE(P-16:0/20:5)	Pos	6.34	722.5127	[M+H]+	Ether-PE	MS/MS	4.58	0.0000	1.46

48hr	1219	PE(P-16:0/22:5)	Neg	7.84	748.5311	[M-H]-	Ether-PE	MS/MS	3.28	0.0000	2.42
48hr	1253	PE(P-18:0/20:1)	Neg	13.52	756.5933	[M-H]-	Ether-PE	MS/MS	2.15	0.0017	1.19
48hr	1325	PE(P-18:0/22:6)	Neg	9.46	774.55	[M-H]-	Ether-PE	MS/MS	4.69	0.0000	1.15
48hr	1212	PG(16:0/18:1)	Neg	6.37	747.5214	[M-H]-	PG	MS/MS	2.10	0.0007	1.12
48hr	1503	PG(18:2/22:6)	Neg	3.59	817.5042	[M-H]-	PG	MS/MS	2.95	0.0010	0.57
48hr	1578	PG(19:1-17:2)	Pos	8.25	790.5621	[M+NH4]+	PG	MS/MS	3.52	0.0000	1.79
48hr	1556	PI(16:1/18:1)	Neg	4.77	833.5212	[M-H]-	PI	MS/MS	0.17	0.0056	1.17
48hr	1645	PI(18:1/18:1)	Neg	6.10	861.5536	[M-H]-	PI	MS/MS	0.47	0.0059	2.14
48hr	1708	PI(18:1/20:3)	Neg	6.14	885.5534	[M-H]-	PI	MS/MS	6.34	0.0000	2.35
48hr	1382	PS(18:0/18:1)	Neg	8.10	788.5485	[M-H]-	PS	MS/MS	2.94	0.0000	4.80

MSMS = lipids that were confirmed with fragment pattern of database; STD = lipids that were confirmed with authentic standards; The 'O-' prefix is used to indicate the presence of an alkyl ether substituent, e.g., PC (O-16:0/0:0), whereas the 'P-' prefix is used for the 1Z-alkenyl ether (Plasmalogen) substituent, e.g., PE (P-16:0/16:0). Abbreviations: Cer, ceramide; CL, cardiolipin; DG, diacylglycerol; EtherLPC, ether-linked lysophosphatidylcholine; EtherPC, ether-linked phosphatidylcholine; EtherLPE, ether-linked lysophosphatidylethanolamine; EtherPE, ether-linked phosphatidylethanolamine; FFA, free fatty acid; LPC, lysophosphatidylcholine; LPE, lysophosphatidylethanolamine; LPG, LysophosphatidylglycerolPC, phosphatidylcholine; PE, phosphatidylethanolamine; PG, phosphatidylglycerol; PI, phosphatidylinositol; PS, phosphatidylserine; SM, sphingomyelin; SPB, sphingoid base. The highlight pink label represents reproducible lipids in different infection time.

Table S3. Targeted metabolites' concentration in linoleic acid metabolism pathway upon exogenous linoleic acid addition

Lipids	Averaged concentration (μM) , sample number =3				Fold change	
	Mock	Mock+LA	Infect	Infect +LA	Mock+LA/Mock	Infect+LA/Infect
Linoleic acid	0.39	5.65	0.31	6.06	14.32	19.42
ᵞ-Linoleic acid	0.03	0.39	0.03	0.35	12.88	10.24
Arachidonic acid	0.09	2.45	0.1	2.27	25.82	23.67
(±)9-HODE	0.05	0.17	0.06	0.23	3.54	4.06
(±)13-HODE	0.12	0.68	0.16	0.99	5.66	4.49
12(13)-EpOME	0.06	0.69	0.02	0.98	16.22	19.98
9(10)-EpOME	3.26	5.83	2.51	5.15	1.79	2.05

Mock represents non-infected cells and infect represents *S. aureus* infected cells.

Table S4. Gradient elution program applied for untargeted lipidomics analysis

Time(min)	Flow rate (mL/min)	Mobile phase A (%)	Mobile phase B (%)	Curve
Initial	0.4	60%	40%	6
2	0.4	57%	43%	6
2.1	0.4	50%	50%	6
12	0.4	46%	54%	6
12.1	0.4	30%	70%	6
18	0.4	1%	99%	6
18.1	0.4	60%	40%	6
20	0.4	60%	40%	6

The mobile phase A was 60:40 acetonitrile:water (v/v) with 10 mM ammonium formate and 0.1% formic acid. The mobile phase B for positive mode was 90:10 isopropanol:acetonitrile (v/v) with 10 mM ammonium formate and 0.1% formic acid. The mobile phase B for negative mode was 90:10 isopropanol:acetonitrile (v/v) with 10 mM ammonium acetate

Table S5. Gradient elution program applied for target lipidomics analysis

Time (min)	Flow rate (mL/min)	Mobile phase A (%)	Mobile phase B (%)
Initial	0.4	53%	47%
9	0.4	53%	47%
9.1	0.4	45%	55%
12	0.4	45%	55%
12.1	0.4	0%	100%
15	0.4	0%	100%
15.1	0.4	53%	47%
17	0.4	53%	47%

The mobile phase A was 0.1% acetic acid in water. The mobile phase B was ACN/IPA (90/10 v/v).

Table S6. List of MRM transitions (M1=precursor; M2= fragment) and retention times for targeted lipids

Lipid name	Retention time (min)	M1	M2
(±)9-HODE	16.19	295.2273	171.1024
(±)13-HODE	15.64	295.2273	195.1376
12(13)-EpOME	16.12	295.2273	195.1376
9(10)-EpOME	13.26	295.2273	183.1
Linoleic acid	13.65	279.2324	261.2204
ᵞ-Linoleic acid	9.97	277.2168	259.2053
Arachidonic acid	9.45	303.2324	259.2411
Arachidonic acid-d8	16.1	311.222	267.24