Untargeted lipidomics reveals specific lipid abnormalities in systemic lupus erythematosus

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Supplementary material

1. Supplementary Data

Methods

Chemicals and materials

Liquidchromatography-grade acetonitrile (ACN), methanol (MeOH) and methyl t-butyl ether (MTBE) were purchased from Merck (Darmstadt, Germany). Isopropyl alcohol, formic acid and ammonium formate were purchased from ROE(DE, USA). Methylbenzene was purchased from Shanghai Lingfeng Chemical Reagent Co., Ltd. Ultrapure water was prepared using a Milli-Q system (Millipore; Billerica, MA, USA).Internal standards (ISs) containing C17-ceramide(Cer)(17:0), lysophosphatidylcholine (LPC) (17:0), lysophosphatidylethanolamine (LPE) (17:1), phosphatidylethanolamine (PE) (17:0/17:0), sphingomyelin (SM) (17:0), triglyceride (TG) (17:0/17:1/17:0), and diacylglycerol (DG) (12:0/12:0/0:0) were obtained from Avanti Polar Lipids (Alabaster, AL). The ISs were prepared in methanol as a stock solution and stored at -20 °C. The concentrations of the ISs were 2.5 μg/mL.

2. Supplementary Figures and Tables

Supplementary Table S1. Differential lipid metabolites between HCs and SLE in the Discovery Set.

metabolites	VIP	*p*-value	FDR
ACar(11:0)	1.143	0.006	0.014
ACar(12:0)	1.068	0.010	0.020
ACar(16:3)	1.764	<0.001	<0.001
ACar(18:2)	1.129	0.016	0.032
ACar(20:1)	1.226	<0.001	<0.001
Cer/NS(d18:2:24:0)	1.436	0.002	0.005
DAG(16:0/18:2)	1.079	<0.001	<0.001
DAG(16:0/18:3)	1.358	<0.001	<0.001
DAG(18:0/18:2)	1.466	<0.001	<0.001
DAG(18:1/18:2)	1.195	<0.001	<0.001
DAG(18:1/20:4)	1.714	<0.001	<0.001
DAG(18:2/18:3)	1.156	<0.001	0.001
DAG(18:2/20:4)	1.222	0.002	0.005
HexCer(40:12O)	1.222	0.001	0.003
HexCer(42:22O)	1.662	<0.001	<0.001
HexCer/NS(d18:1:24:1)	1.123	0.001	0.004
LPC(14:0)	1.453	<0.001	<0.001
LPC(15:0)	1.028	<0.001	0.002
LPC(15:0(SN2))	1.407	<0.001	<0.001
LPC(16:0)	1.425	<0.001	<0.001
LPC(16:2e)	1.784	<0.001	<0.001
LPC(18:0)	1.914	<0.001	<0.001
LPC(18:1)	1.238	<0.001	<0.001
LPC(18:2)	1.409	<0.001	<0.001
LPC(18:3(SN2))	1.040	0.003	0.008
LPC(18:4e)	1.064	0.001	0.004
LPC(20:3)	1.033	0.001	0.003
LPC(20:3e)	1.315	<0.001	0.001
LPC(20:4)	1.393	<0.001	<0.001
LPC(22:1e)	1.628	<0.001	<0.001
LPC(22:5))	1.517	<0.001	<0.001
LPC(22:6)	1.431	<0.001	<0.001
LPC(24:2e)	1.278	0.004	0.009
LPE(16:1e)	1.243	<0.001	<0.001
LPE(17:1)	1.029	0.014	0.027
LPE(18:0)	1.961	<0.001	<0.001
LPE(18:2)	1.520	<0.001	<0.001
LPE(20:4)	1.740	<0.001	<0.001

PC(14:0/18:2)	1.123	0.001	0.003
PC(14:0e:10:0)	1.258	<0.001	0.001
PC(14:0e:22:3)	1.310	0.001	0.003
PC(14:1e:10:0)	1.613	<0.001	<0.001
PC(14:1e:3:0)	1.564	<0.001	<0.001
PC(14:1e:5:0)	1.134	<0.001	<0.001
PC(16:0e:22:5)	1.171	<0.001	<0.001
PC(18:0/20:3)	1.083	0.005	0.013
PC(18:1e:22:6)	1.190	<0.001	0.001
PC(18:4e:2:0)	1.371	<0.001	<0.001
PC(18:5e:2:0)	1.141	0.002	0.005
PC(20:5e:2:0)	1.420	<0.001	<0.001
PC(22:1/18:4)	1.263	<0.001	0.002
PC(22:4e:2:0)	2.309	<0.001	<0.001
PC(34:3)	1.316	0.001	0.002
PC(36:3)	1.808	<0.001	<0.001
PC(36:5)	1.054	0.007	0.016
PC(38:3)	2.179	<0.001	<0.001
PC(38:5)	1.189	0.010	0.021
PE(16:0/18:2)	2.546	<0.001	<0.001
PE(16:1/22:5)	2.184	<0.001	<0.001
PE(18:0/18:2)	1.265	<0.001	<0.001
PE(18:0e:20:5)	1.240	0.013	0.026
PE(18:2/18:2)	1.612	<0.001	<0.001
PE 20:3/20:3)	2.087	<0.001	<0.001
PE(38:5)	2.540	<0.001	<0.001
PI(36:3)	1.663	<0.001	<0.001
SM(34:0;2O)	1.767	<0.001	<0.001
SM(34:2;2O)	1.599	<0.001	<0.001
SM(36:1;2O)	1.170	0.003	0.008
SM(36:2;2O)	1.043	0.004	0.009
SM(40:3;2O)	1.282	0.002	0.005
SM(42:2;2O)	1.564	<0.001	<0.001
SM(42:3;2O)	1.421	0.001	0.002
SM(d14:0:20:0)	1.230	<0.001	<0.001
SM(d14:0:22:0)	1.337	<0.001	0.002
SM(d14:1:18:1)	1.142	0.001	0.004
Sphinganine(26:0)	2.275	<0.001	<0.001
TAG(12:0/12:0/16:0)	1.253	0.019	0.037
TAG(12:0/12:0/18:1)	1.976	<0.001	<0.001
TAG(12:0/12:0/18:2)	1.613	<0.001	<0.001
TAG(12:0/13:0/17:1)	1.798	<0.001	<0.001
TAG(12:0/14:0/14:1)	1.570	<0.001	0.001
TAG(12:0/14:0/15:0)	2.258	<0.001	<0.001

TAG(12:0/14:0/16:0)	1.559	<0.001	<0.001
TAG(12:0/14:0/16:1)	1.758	<0.001	<0.001
TAG(12:0/14:0/18:1)	2.009	<0.001	<0.001
TAG(12:0/15:0/16:0)	2.327	<0.001	<0.001
TAG(12:0/16:0/16:1)	1.197	0.008	0.018
TAG(12:0/16:0/18:2)	1.126	0.003	0.008
TAG(12:0/16:0/18:3)	1.470	<0.001	<0.001
TAG(13:0/14:0/14:0)	2.211	<0.001	<0.001
TAG(13:0/14:0/16:0)	1.987	<0.001	<0.001
TAG(13:0/14:0/16:1)	2.139	<0.001	<0.001
TAG(13:0/14:1/16:1)	2.289	<0.001	<0.001
TAG(14:0/14:0/15:0)	2.155	<0.001	<0.001
TAG(14:0/14:0/16:0)	1.549	<0.001	<0.001
TAG(14:0/14:1/15:0)	2.040	<0.001	<0.001
TAG(14:0/14:1/16:1)	1.214	0.002	0.006
TAG(14:0/15:0/16:0)	2.424	<0.001	<0.001
TAG(14:0/15:0/16:1)	2.172	<0.001	<0.001
TAG(14:0/15:1/16:1)	2.078	<0.001	<0.001
TAG(14:0/16:0/16:0)	1.816	<0.001	<0.001
TAG(14:0/16:0/16:1)	1.471	<0.001	0.001
TAG(14:0/16:0/17:0)	2.146	<0.001	<0.001
TAG(14:0/16:0/18:3)	1.494	0.001	0.003
TAG(14:0/16:0/22:6)	1.062	0.006	0.014
TAG(14:0/16:1/16:1)	1.291	<0.001	<0.001
TAG(14:0/18:0/22:0)	1.375	<0.001	<0.001
TAG(14:1/15:0/15:0)	1.988	<0.001	<0.001
TAG(14:1/16:1/16:1)	1.594	<0.001	<0.001
TAG(15:0/15:0/16:0）	1.825	<0.001	<0.001
TAG(15:0/16:0/16:0）	1.991	<0.001	<0.001
TAG(15:0/16:0/16:1）	2.077	<0.001	<0.001
TAG(15:0/16:0/18:0）	1.692	<0.001	<0.001
TAG(15:0/16:0/18:1）	1.088	<0.001	0.001
TAG(15:0/16:0/18:3）	1.286	0.003	0.009
TAG(15:0/16:1/16:1）	2.209	<0.001	<0.001
TAG(15:1/16:1/16:1）	2.373	<0.001	<0.001
TAG(16:0/16:0/17:0）	1.681	<0.001	<0.001
TAG(16:0/16:0/22:6）	1.396	0.002	0.006
TAG(16:0/18:0/20:0）	1.802	<0.001	<0.001
TAG(16:0/18:1/22:0）	1.801	<0.001	<0.001
TAG(16:0/18:1/22:5）	1.348	<0.001	<0.001
TAG(16:0/18:1/22:6）	1.178	<0.001	<0.001
TAG(16:0/18:2/18:4）	1.091	<0.001	0.001
TAG(16:0/18:2/20:5)	1.500	<0.001	<0.001

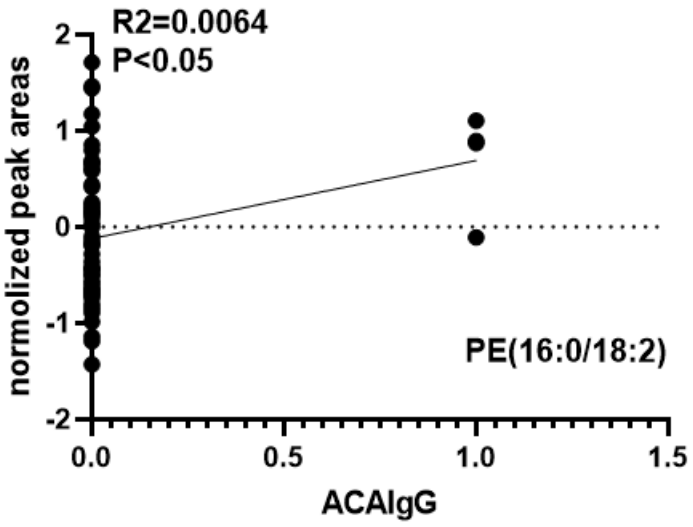
TAG(16:0/18:2/22:5)	1.130	<0.001	<0.001
TAG(16:0/18:2/22:6)	1.015	0.001	0.003
TAG(16:0/20:0/20:0)	2.009	<0.001	<0.001
TAG(16:1/18:1/20:5)	1.309	<0.001	<0.001
TAG(17:0/18:0/18:1)	1.109	0.001	0.003
TAG(17:0/18:1/18:2)	1.556	<0.001	<0.001
TAG(18:0/18:0/18:0)	1.289	<0.001	<0.001
TAG(18:0/18:0/20:4)	1.215	0.002	0.006
TAG(18:0/18:0/22:5)	1.143	0.001	0.002
TAG(18:0/18:1/19:1)	1.697	<0.001	<0.001
TAG(18:0/18:1/20:5)	1.233	0.001	0.004
TAG(18:0/18:1/22:1)	1.389	0.001	0.004
TAG(18:0/18:2/22:5)	1.084	<0.001	<0.001
TAG(18:1/18:1/22:4)	1.659	<0.001	<0.001
TAG(18:1/18:1/22:5)	1.105	<0.001	<0.001
TAG(18:1/18:1/22:6)	1.101	<0.001	<0.001
TAG(18:1/18:2/20:1)	1.672	<0.001	<0.001
TAG(18:1/18:2/20:2）	1.248	<0.001	<0.001
TAG(18:1/18:2/20:3）	1.543	<0.001	<0.001
TAG(18:1/18:2/22:4）	1.442	<0.001	<0.001
TAG(18:1/18:2/22:6）	1.274	0.001	0.003
TAG(18:1/20:0/22:1）	1.545	0.001	0.004
TAG(18:1/22:1/22:1）	1.069	0.017	0.033
TAG(18:2/18:2/20:3）	1.316	<0.001	<0.001
TAG(18:2/18:2/20:5）	1.092	0.001	0.004
TAG(18:2/18:2/22:5）	1.135	0.001	0.003
TAG(18:2/18:3/22:1）	1.189	<0.001	<0.001
TAG(18:2/20:4/22:6）	1.562	<0.001	<0.001
TAG(19:0/19:0/19:1）	1.923	<0.001	<0.001
TAG(20:1/22:1/22:1）	2.024	<0.001	<0.001
TAG(22:1/22:1/22:1）	2.034	<0.001	<0.001

Supplementary Table S2. Differential metabolites between HCs and SLE in the Discovery set and Validation set.

Metabolite	Discovery Set				Validation set			
	VIP	*p*-value	FDR	FC	VIP	*p*-value	FDR	FC
ACar(11:0)	1.143	0.006	0.014	0.777	2.082	<0.001	<0.001	0.132
ACar(12:0)	1.068	0.010	0.020	0.836	1.498	<0.001	<0.001	0.377
DAG(16:0/18:2)	1.079	<0.001	<0.001	1.976	1.727	<0.001	<0.001	2.002
DAG(16:0/18:3)	1.358	<0.001	<0.001	2.477	1.270	<0.001	<0.001	2.060
DAG(18:0/18:2)	1.466	<0.001	<0.001	2.022	1.363	<0.001	<0.001	2.101
DAG(18:1/18:2)	1.195	<0.001	<0.001	1.982	1.564	<0.001	<0.001	1.718
DAG(18:1/20:4)	1.714	<0.001	<0.001	1.874	1.478	<0.001	<0.001	2.199
DAG(18:2/20:4)	1.222	0.002	0.005	0.815	1.331	<0.001	<0.001	0.746
HexCer/NS(d18:1/24:1)	1.123	0.001	0.004	1.726	1.626	<0.001	<0.001	2.395
LPC(16:2e)	1.784	<0.001	<0.001	1.581	1.235	<0.001	<0.001	1.527
LPE(18:0)	1.961	<0.001	<0.001	1.840	2.171	<0.001	<0.001	2.967
LPE(20:4)	1.740	<0.001	<0.001	1.629	1.193	<0.001	<0.001	1.529
PC(14:1e/10:0)	1.613	<0.001	<0.001	1.661	1.189	<0.001	<0.001	2.064
PC(14:1e/5:0)	1.134	<0.001	<0.001	1.488	1.470	<0.001	<0.001	1.804
PE(16:0/18:2)	2.546	<0.001	<0.001	2.926	2.161	<0.001	<0.001	5.858
PE(16:1/22:5)	2.184	<0.001	<0.001	2.093	2.026	<0.001	<0.001	3.277
PE(18:0/18:2)	1.265	<0.001	<0.001	2.069	1.671	<0.001	<0.001	2.896
PE(18:2/18:2)	1.612	<0.001	<0.001	3.312	1.384	<0.001	<0.001	5.442
PE(20:3/20:3)	2.087	<0.001	<0.001	2.086	2.003	<0.001	<0.001	3.558
PE(38:5)	2.540	<0.001	<0.001	2.675	1.978	<0.001	<0.001	3.101
SM(34:0;2O)	1.767	<0.001	<0.001	1.660	1.588	<0.001	<0.001	1.758
SM(34:2;2O)	1.599	<0.001	<0.001	1.486	1.099	<0.001	<0.001	1.261
SM(36:1;2O)	1.170	0.003	0.008	1.318	1.384	<0.001	<0.001	1.659
SM(36:2;2O)	1.043	0.004	0.009	1.325	1.201	<0.001	<0.001	1.345
SM(42:2;2O)	1.564	<0.001	<0.001	1.515	1.472	<0.001	<0.001	1.713
SM(42:3;2O)	1.421	<0.001	0.002	1.321	1.468	<0.001	<0.001	1.498
SM(d14:0/20:0)	1.230	<0.001	<0.001	1.467	1.628	<0.001	<0.001	1.817
SM(d14:0/22:0)	1.337	<0.001	0.002	1.568	1.444	<0.001	<0.001	3.428
TAG(12:0/13:0/17:1)	1.798	<0.001	<0.001	0.640	1.073	<0.001	<0.001	0.674

TAG(12:0/14:0/15:0)	2.258	<0.001	<0.001	0.533	1.656	<0.001	<0.001	0.397
TAG(12:0/14:0/16:1)	1.758	<0.001	<0.001	0.662	1.343	<0.001	<0.001	0.562
TAG(12:0/15:0/16:0)	2.327	<0.001	<0.001	0.555	1.905	<0.001	<0.001	0.449
TAG(12:0/16:0/16:1)	1.197	0.008	0.018	0.709	1.334	<0.001	<0.001	0.324
TAG(13:0/14:0/14:0)	2.211	<0.001	<0.001	0.548	1.649	<0.001	<0.001	0.570
TAG(13:0/14:0/16:0)	1.987	<0.001	<0.001	0.632	1.613	<0.001	<0.001	0.465
TAG(13:0/14:0/16:1)	2.139	<0.001	<0.001	0.588	2.004	<0.001	<0.001	0.435
TAG(13:0/14:1/16:1)	2.289	<0.001	<0.001	0.553	1.962	<0.001	<0.001	0.279
TAG(14:0/14:0/15:0)	2.155	<0.001	<0.001	0.614	1.878	<0.001	<0.001	0.457
TAG(14:0/14:0/16:0)	1.549	<0.001	<0.001	0.907	1.454	<0.001	<0.001	0.611
TAG(14:0/14:1/15:0)	2.040	<0.001	<0.001	0.626	1.649	<0.001	<0.001	0.528
TAG(14:0/15:0/16:0)	2.424	<0.001	<0.001	0.511	2.155	<0.001	<0.001	0.324
TAG(14:0/15:0/16:1）	2.172	<0.001	<0.001	0.519	2.053	<0.001	<0.001	0.454
TAG(14:0/15:1/16:1)	2.078	<0.001	<0.001	0.550	1.459	<0.001	<0.001	0.501
TAG(14:0/16:0/16:0)	1.816	<0.001	<0.001	0.741	1.374	<0.001	<0.001	0.682
TAG(14:0/16:0/16:1)	1.471	<0.001	0.001	0.780	1.793	<0.001	<0.001	0.510
TAG(14:0/16:0/17:0)	2.146	<0.001	<0.001	0.608	1.582	<0.001	<0.001	0.477
TAG(14:0/16:0/18:3)	1.494	0.001	0.003	0.747	1.576	<0.001	<0.001	0.393
TAG(14:0/16:1/16:1)	1.291	< 0.001	< 0.001	0.633	1.213	<0.001	<0.001	0.563
TAG(14:0/18:0/22:0)	1.375	< 0.001	< 0.001	0.686	1.218	<0.001	<0.001	0.506
TAG(14:1/15:0/15:0)	1.988	< 0.001	< 0.001	0.572	1.023	<0.001	<0.001	0.707
TAG(15:0/15:0/16:0)	1.825	< 0.001	< 0.001	0.803	1.031	<0.001	<0.001	0.713
TAG(15:0/16:0/16:0)	1.991	< 0.001	< 0.001	0.621	1.871	<0.001	<0.001	0.527
TAG(15:0/16:0/16:1)	2.077	< 0.001	< 0.001	0.599	2.035	<0.001	<0.001	0.438
TAG(15:0/16:0/18:0)	1.692	< 0.001	< 0.001	0.707	1.440	<0.001	<0.001	0.558
TAG(15:0/16:0/18:1)	1.088	< 0.001	0.001	0.723	1.012	<0.001	0.001	0.779
TAG(15:0/16:0/18:3)	1.286	0.003	0.009	0.742	1.347	<0.001	<0.001	0.493
TAG(15:0/16:1/16:1)	2.209	<0.001	<0.001	0.607	1.491	<0.001	<0.001	0.557
TAG(15:1/16:1/16:1)	2.373	<0.001	<0.001	0.536	1.915	<0.001	<0.001	0.421
TAG(16:0/16:0/17:0)	1.681	<0.001	<0.001	0.617	1.016	0.001	0.001	0.697
TAG(16:0/18:0/20:0)	1.802	<0.001	<0.001	0.678	1.825	<0.001	<0.001	0.570
TAG(16:0/18:1/22:0)	1.801	<0.001	<0.001	0.670	1.964	<0.001	<0.001	0.554
TAG(16:0/18:1/22:5)	1.348	<0.001	<0.001	1.784	1.802	<0.001	<0.001	2.087

TAG(16:0/20:0/20:0)	2.009	<0.001	<0.001	0.550	1.714	<0.001	<0.001	0.619
TAG(17:0/18:1/18:2)	1.556	<0.001	<0.001	1.631	1.133	<0.001	<0.001	1.488
TAG(18:0/18:0/22:5)	1.143	0.001	0.002	1.748	1.733	<0.001	<0.001	2.147
TAG(18:0/18:1/19:1)	1.697	<0.001	<0.001	0.663	1.156	<0.001	<0.001	0.684
TAG(18:1/18:1/22:4)	1.659	<0.001	<0.001	2.360	1.557	<0.001	<0.001	1.947
TAG(18:1/18:2/20:1)	1.672	<0.001	<0.001	1.888	1.754	<0.001	<0.001	2.436
TAG(18:1/18:2/20:2)	1.248	<0.001	<0.001	1.633	1.347	<0.001	<0.001	1.742
TAG(18:1/18:2/20:3)	1.543	<0.001	<0.001	2.137	1.492	<0.001	<0.001	2.608
TAG(18:1/18:2/22:4)	1.442	<0.001	<0.001	1.672	1.435	<0.001	<0.001	1.923
TAG(18:1/20:0/22:1)	1.545	0.001	0.004	0.733	1.382	<0.001	<0.001	0.744
TAG(18:2/18:3/22:1)	1.189	<0.001	<0.001	1.820	1.331	<0.001	<0.001	1.799
TAG(19:0/19:0/19:1)	1.923	<0.001	<0.001	0.597	2.001	<0.001	<0.001	0.541
TAG(20:1/22:1/22:1)	2.024	<0.001	<0.001	0.584	1.623	<0.001	<0.001	0.419
TAG(22:1/22:1/22:1)	2.034	<0.001	<0.001	0.535	1.691	<0.001	<0.001	0.285



Supplementary Fig. S1. Spearman correlation analysis between PE (16:0/18:2) and ANA IgG.