Supplemental data

A distinct glycerophospholipid metabolism signature of acute graft versus host disease with predictive value

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Supplemental Methods

Included criteria for alloHSCT patients

In discovery phase, 67 patients with hematologic malignancies received HLA-matched alloHSCT at Department of Hematology, Changhai Hospital between September 2014 and May 2016 were retrospectively analyzed. Another group of 61 patients who received HLA-matched alloHSCT between June 2016 and June 2018 were included in validation group. Patients who relapsed after alloHSCT within 6 months (n=21, 10 patients in discovery group and 11 patients in validation group, respectively.) were excluded from the study. The last follow-up was December 31st, 2018.

Sample preparation for LC-MS analysis

For RPLC-MS analysis, 400 μL of methanol/ACN (1:1; containing 0.005 mg/mL L-2-chlorophenylalanine as the internal standard) was added to 100 μL aliquots of serum. For HILIC-MS analysis, 400 μL of methanol/ethanol (1:1; containing 0.005 mg/mL L-2-chlorophenylalanine as the internal standard) was added to 100 μL aliquots of serum. The mixture was vortex-mixed vigorously for 30 s and subsequently centrifuged at 14,000g for 15 min at 4℃. The supernatant was transferred to autosampler vial and an aliquot of 4 μL was injected for LC-MS

analysis. An in-house quality control (QC) was prepared by pooling and mixing the same volume of each sample.

Data acquisition

In this study, an Agilent 1290 Infinity LC system configured with an Agilent 6530 Accurate-Mass Quadrupole Time-of-Flight (Q-TOF) mass spectrometer (Agilent, USA) was used to perform the LC-MS analysis. For RP analysis, an acquity UPLC HSS T3 column (2.1 mm × 100 mm, 1.8 μm, Waters, Milford, MA) was used for the reversed phase separation. The mobile phase consisted of 0.1% formic acid (A) and ACN modified with 0.1% formic acid (B), using a gradient elution of 5%B at 0–2 min, 5%–95% B at 2–13min, 95% B at 13–15 min. The total run time was 20 min including equilibration. The flow rate was 350 μL/min and the injection volume was 4 μL. For HILIC analysis, an acquity UPLC BEH HILIC column (2.1 mm × 100 mm, 1.7 μm, Waters, Milford, MA) was used on the same LC system as above. The mobile phase consisted of 10 mM ammonium formate modified with 0.1% formic acid (A) and ACN/H2O (95:5, v/v) modified with 0.1% formic acid (B), using a gradient elution of 95%B at 0–2 min, 95%–89% B at 2–4 min, 89% B at 4–13.5 min, 89%–66% B at 13.5–15 min, 66% B at 15–17 min. The total run time was 24 min including equilibration. The flow rate was 350 μL/min and the injection volume were 4 μL.

An electrospray ionization source (ESI) interface was used and was set in positive mode. The following parameters were employed: capillary voltage, 3.5 kV; drying gas flow, 11 L/min; gas temperature: 350 °C; nebulizer pressure, 45 psig. fragmentor voltage, 120 V; skimmer voltage, 60 V. Data were collected in centroid mode and the mass range was set at m/z 50–1000 using extended dynamic range. The MS/MS spectra of metabolites were obtained by a collision energy ramp from 10−30 eV.

Identification of biomarker metabolites

The selected biomarker metabolites were further identified by comparison of tandem mass spectra (MS/MS) and retention time (RT) with those of reference standards, and those available in libraries including HMDB (http://www.hmdb.ca), METLIN (http://metlin.scripps.edu), the mass bank Web site (http://www.massbank.jp/en/database.html) and LIPID MAPS (http://www.lipidmaps.org).

Supplemental Table S1. Summary of potential biomarkers of aGvHD by RPLC-MS and HILIC-MS analysis

					Training set		Validation set	
Identification	Column	Formula	Trend	Related pathway	P value	Fold change	P value	Fold change
LysoPC(16:0)	RP	C24H50NO7P	↓	Glycerophospholipid metabolism	7.74E-03	0.68	1.62E-02	0.71
PC(16:0/22:6)	RP	C46H80NO8P	↑	Glycerophospholipid metabolism	7.46E-03	1.57	1.41E-02	1.42
PE(20:4/20:3)	RP	C42H80NO10P	↑	Glycerophospholipid metabolism; Glycosylphosphatidylinositol-anchor biosynthesis	7.54E-03	1.57	5.99E-04	1.80
L-Phenylalanine	RP	C9H11NO2	↑	Phenylalanine metabolism; Aminoacyl-tRNA biosynthesis	5.42E-03	1.31	2.54E-02	1.34
LysoPC(20:3)	RP	C28H52NO7P	↓	Glycerophospholipid metabolism	6.12E-04	0.78	1.40E-03	0.56
PC(13:0/0:0)	RP	C21H44NO7P	↑	Glycerophospholipid metabolism	5.95E-03	1.43	2.03E-04	1.56
Elaidic carnitine	RP	C25H47NO4	↓	Fatty acid β-oxidation	4.02E-02	0.73	4.59E-02	0.81
3α,7α,12α-trihydroxy-27-carboxymethyl-5β-cholestan-26-oic acid	RP	C29H48O7	↓	Bile acid metabolism	2.91E-03	0.76	1.58E-02	0.56
Uric acid	RP	C5H4N4O3	↓	Purine metabolism	1.96E-02	0.78	1.55E-02	0.72
LysoPE(0:0/22:4)	RP	C27H48NO7P	↓	Glycerophospholipid metabolism	6.08E-04	0.78	5.10E-04	0.63
TG(17:1/22:1/22:3)	RP	C64H114O6	↓	Glycerolipid metabolism	1.49E-02	0.71	1.61E-02	0.73
SM(d16:1/17:0)	RP	C38H77N2O6P	↑	Sphingolipid metabolism	2.83E-02	1.32	4.80E-03	1.10
L-Valine	RP	C5H11NO2	↓	Valine, Leucine and Isoleucine Degradation; Aminoacyl-tRNA biosynthesis	3.21E-02	0.76	3.93E-02	0.70
Stearoylcarnitine	RP	C25H49NO4	↓	Fatty acid β-oxidation	1.89E-02	0.73	3.47E-02	0.64
DG(21:0/22:4/0:0)	RP	C46H82O5	↓	Glycerophospholipid metabolism	1.16E-03	0.62	3.60E-02	0.77
L-Carnitine	RP	C7H15NO3	↑	Fatty acid β-oxidation	2.29E-03	1.25	4.39E-04	1.62
Propionylcarnitine	RP	C10H19NO4	↑	Propanoate metabolism; Fatty acid β-oxidation	2.43E-02	1.46	3.40E-02	1.37
LysoPC(17:0)	RP	C25H52NO7P	↓	Glycerophospholipid metabolism	1.98E-03	0.76	4.00E-03	0.52

Phytosphingosine	RP	C18H39NO3	↓	Sphingolipid metabolism	3.46E-03	0.68	1.03E-02	0.73
4-hydroxy palmitic acid	RP	C16H32O3	↓	Fatty acid metabolism	4.45E-02	0.84	8.95E-03	0.86
LysoPC(18:2)	HILIC	C26H50NO7P	↓	Glycerophospholipid metabolism	8.72E-03	0.83	2.14E-02	0.79
PC(14:0/18:1)	HILIC	C40H78NO8P	↑	Glycerophospholipid metabolism	2.21E-02	1.88	3.95E-02	1.79
LysoPC(18:1)	HILIC	C26H52NO7P	↓	Glycerophospholipid metabolism	2.03E-02	0.81	2.46E-02	0.76
PC(15:0/20:5)	HILIC	C43H76NO8P	↑	Glycerophospholipid metabolism	3.20E-02	1.68	2.47E-02	1.73
C16:0 PAF	HILIC	C26H54NO7P	↓	Glycerophospholipid metabolism	1.17E-04	0.55	8.98E-05	0.52
LysoPE(0:0/20:1)	HILIC	C25H50NO7P	↓	Glycerophospholipid metabolism	1.15E-02	0.67	3.96E-02	0.72
Citric acid	HILIC	C6H8O7	↓	Citrate cycle; Alanine, aspartate and glutamate metabolism	2.06E-02	0.70	3.49E-02	0.79
L-Glutamine	HILIC	C5H10N2O3	↓	D-Glutamine and D-glutamate metabolism; Aminoacyl-tRNA biosynthesis; Alanine, aspartate and glutamate metabolism ; Nitrogen metabolism	1.29E-03	0.73	7.13E-03	0.73
2-hydroxy behenic	HILIC	C22H44O3	↓	Fatty acid metabolism	5.33E-03	0.80	1.33E-02	0.82
Arachidic Acid	HILIC	C20H40O2	↓	Arachidonic acid metabolism	3.24E-02	0.85	1.87E-02	0.81
LysoPC(22:6)	HILIC	C30H50NO7P	↓	Glycerophospholipid metabolism	1.88E-04	0.63	4.13E-05	0.49
PE(16:0/18:2)	HILIC	C39H74NO8P	↑	Glycerophospholipid metabolism; Glycosylphosphatidylinositol-anchor biosynthesis	5.90E-03	1.72	4.09E-03	1.65
LysoPC (P-16:0)	HILIC	C24H50NO6P	↓	Glycerophospholipid metabolism	5.24E-04	0.68	1.71E-02	0.61
5-Oxoproline	HILIC	C5H7NO3	↓	Glutathione metabolism; Arginine and proline metabolism	1.74E-03	0.74	5.69E-03	0.78
2-oxo-heneicosanoic acid	HILIC	C21H40O3	↓	Fatty acid metabolism	6.67E-04	0.74	2.24E-03	0.72
Cerebronic acid	HILIC	C24H48O3	↓	Fatty acid metabolism	4.05E-03	0.81	5.67E-03	0.82
Biopterin	HILIC	C9H11N5O3	↑	Folate biosynthesis	3.41E-02	3.21	1.91E-02	1.81
Behenic acid	HILIC	C22H44O2	↓	Fatty acid metabolism	2.12E-02	0.83	2.67E-02	0.85

Abbreviations: LysoPC, lysophosphatidylcholine; PC, phosphatidylcholine; PE, phosphatidylethanolamine; TG, triacylglycerol; SM, sphingomyelin; DG, diacylglycerol; LysoPE, lysophosphatidylethanolamine.

Supplemental Table S2. **Metabolites between aGvHD group and aGvHD in remission group (aGvHD$^{\triangle}$)**

Metabolite	Column	Formula	Training set		Validation set	
			P value	FC[a]	P value	FC[a]
LysoPC(16:0)	RP	C24H50NO7P	1.54E-02	1.32	1.75E-03	1.52
PC(16:0/22:6)	RP	C46H80NO8P	5.33E-01	0.89	1.09E-02	0.43
PE(20:4/20:3)	RP	C42H80NO10P	1.78E-01	0.76	4.23E-02	0.78
L-Phenylalanine	RP	C9H11NO2	3.31E-01	1.14	5.21E-01	0.93
LysoPC(20:3)	RP	C28H52NO7P	1.99E-04	1.83	9.68E-03	1.78
PC(13:0/0:0)	RP	C21H44NO7P	4.37E-02	0.76	9.11E-02	0.81
Elaidic carnitine	RP	C25H47NO4	8.79E-01	1.03	2.34E-01	1.65
3α,7α,12α-trihydroxy-27-carboxymethyl-5β-cholestan-26-oic acid	RP	C29H48O7	2.18E-03	1.48	3.90E-02	1.87
Uric acid	RP	C5H4N4O3	8.62E-04	1.49	5.76E-03	1.71
LysoPE(0:0/22:4)	RP	C27H48NO7P	4.30E-03	1.28	1.68E-02	1.46
TG(17:1/22:1/22:3)	RP	C64H114O6	5.52E-03	1.77	6.83E-03	1.70
SM(d16:1/17:0)	RP	C38H77N2O6P	5.70E-02	0.73	7.35E-01	1.06
L-Valine	RP	C5H11NO2	1.36E-01	1.20	8.02E-01	0.97
Stearoylcarnitine	RP	C25H49NO4	1.45E-01	1.28	1.10E-02	1.70
DG(21:0/22:4/0:0)	RP	C46H82O5	8.71E-01	1.03	1.19E-01	1.53
L-Carnitine	RP	C7H15NO3	2.06E-04	0.68	2.77E-01	0.89
Propionylcarnitine	RP	C10H19NO4	6.70E-01	0.92	4.54E-01	1.22
LysoPC(17:0)	RP	C25H52NO7P	2.68E-03	1.46	3.86E-04	2.34
Phytosphingosine	RP	C18H39NO3	6.43E-01	0.92	9.49E-01	1.01
4-hydroxy palmitic acid	RP	C16H32O3	4.76E-02	1.20	1.55E-01	1.18
LysoPC(18:2)	HILIC	C26H50NO7P	4.64E-05	1.38	3.19E-02	1.41
PC(14:0/18:1)	HILIC	C40H78NO8P	1.63E-02	0.60	4.48E-02	0.83
LysoPC(18:1)	HILIC	C26H52NO7P	1.51E-02	1.35	6.20E-02	1.48

PC(15:0/20:5)	HILIC	C43H76NO8P	4.42E-02	0.48	9.95E-03	0.66
C16:0 PAF	HILIC	C26H54NO7P	1.64E-03	2.00	2.10E-04	1.81
LysoPE(0:0/20:1)	HILIC	C25H50NO7P	2.15E-02	1.29	4.11E-02	1.29
Citric acid	HILIC	C6H8O7	2.51E-02	1.68	7.27E-02	1.37
L-Glutamine	HILIC	C5H10N2O3	1.68E-01	1.14	6.91E-02	1.37
2-hydroxy behenic	HILIC	C22H44O3	2.21E-01	1.13	1.50E-01	1.16
Arachidic Acid	HILIC	C20H40O2	4.06E-01	1.10	2.19E-01	1.17
LysoPC(22:6)	HILIC	C30H50NO7P	1.82E-02	1.41	2.07E-04	1.90
PE(16:0/18:2)	HILIC	C39H74NO8P	7.03E-01	0.92	3.50E-01	0.83
LysoPC (P-16:0)	HILIC	C24H50NO6P	1.54E-03	1.82	1.14E-02	1.54
5-Oxoproline	HILIC	C5H7NO3	1.29E-01	1.16	3.52E-02	1.27
2-oxo-heneicosanoic acid	HILIC	C21H40O3	6.47E-01	1.06	1.83E-02	1.22
Cerebronic acid	HILIC	C24H48O3	3.71E-01	1.09	8.31E-03	1.26
Biopterin	HILIC	C9H11N5O3	2.33E-02	0.10	3.47E-02	0.60
Behenic acid	HILIC	C22H44O2	6.71E-01	1.04	1.62E-02	1.19

Abbreviations: FC, fold change; LysoPC, lysophosphatidylcholine; PC, phosphatidylcholine; PE, phosphatidylethanolamine; TG, triacylglycerol; SM, sphingomyelin; DG, diacylglycerol; LysoPE, lysophosphatidylethanolamine.

[a] aGvHD remission group compare to aGVHD group

Supplemental Table S3. **A panel of 5 metabolites with predictive value for aGvHD**

Metabolite	Median, range		AUC in ROC curve		regression weight
	training	validation	training	validation	
v1, PE(20:4/20:3)	0.544(0.156, 2.974)	0.531 (0.157, 1.311)	0.707 (0.571,0.844)	0.891 (0.802,0.980)	2.2974
v2, PC(13:0/0:0)	0.064(0.029, 0.215)	0.114 (0.036, 0.496)	0.689 (0.551-0.827)	0.761 (0.630,0.892)	20.8171
v3, LysoPE(0:0/22:4)	0.037(0.013, 0.057)	0.043 (0.008, 0.107)	0.740 (0.611,0.868)	0.635 (0.479,0.791)	-102.8055
v4, C16:0 PAF	7.113(1.718, 20.903)	8.764 (1.723, 19.750)	0.799 (0.681,0.916)	0.865 (0.768,0.963)	-0.0939
v5, LysoPC(22:6)	2.343(0.518, 6.111)	2.107 (0.429, 6.015)	0.795 (0.679,0.911)	0.790 (0.665,0.915)	-1.1977
GRS	-4.794 (-11.20, 0.498)	-4.839 (-17.185, -1.022)	0.922 (0.849, 0.996)	0.896(0.811, 0.981)	NA

The risk score of aGvHD (GRS) in each sample is calculated by 5 metabolites according to the followed equation:
GRS= 2.2974× v1+20.8171× v2-102.8055× v3-0.0939× v4-1.1977× v5

Supplemental Table S4. Basic characteristics of patients according to GRS

Variable	Training set			Validation set		
	Low (< -4.7427531)	High(≥ -4.7427531)	*P*	Low (< -4.7427531)	High (≥ -4.7427531)	*P*
Number of patients	29	28		25	25	
Age at transplant, yr.	36 (19, 58)	33 (20, 60)	0.707	40 (18,66)	33 (17,54)	0.009
Sex, n (%)			0.357			1.000
Male	17 (58.62)	13 (46.43)		15 (60.00)	15 (60.00)	
Female	12 (41.38)	15 (53.57)		10 (40.00)	10 (40.00)	
Disease status, n (%)			0.957			0.724
CR	27 (93.10)	25 (89.29)		21 (84.00)	19 (76.00)	
NR	2 (6.90)	3 (10.71)		4 (16.00)	6 (24.00)	
Donor age	34 (12, 54)	36.5 (15, 59)	0.240	35 (9, 55)	35.5 (16, 59）	0.708
Donor sex, n (%)			0.501			0.225
Male	22 (75.86)	19 (67.86)		15 (60.00)	19 (76.00)	
Female	7 (24.14)	9 (32.14)		10 (40.00)	6 (24.00)	
ABO, n (%)			0.896			0.771
matched	15 (51.72)	14 (50.0)		10 (40.00)	9 (36.00)	
mismatched	14 (48.28)	14 (50.0)		15 (60.00)	16 (64.00)	
Donor type, n (%)			0.509			0.225
Related	16 (55.17)	13 (46.43)		19 (76.00)	15 (60.00)	
unrelated	13 (44.83)	15 (53.57)		6 (24.00)	10 (40.00)	
Conditioning regimen, n (%)			0.410			1.000
RIC	9 (31.03)	6 (21.43)		2 (8.00)	3 (12.00)	
MAC	20 (68.97)	22 (78.57)		23 (92.00)	22 (88.00)	
CD34+, $x10^6$/Kg	3.05 (1.23, 10.94)	3.25 (0.79, 11.00)	0.943	5.06 (2.51, 10.07)	4.16 (1.34, 10.60)	0.382
MNC, $x10^8$/Kg	6.30 (2.14, 10.74)	6.45 (1.74, 10.32)	0.822	5.97 (1.81, 13.76)	5.00 (1.12, 9.26)	0.216
Composition			<0.0001			0.00002
aGvHD	3 (10.34)	24 (85.71)		4 (16.00)	20 (80.00)	
Without aGvHD	26 (89.66)	4 (14.29)		21 (84.00)	5 (20.00)	
OS, months	31.71±2.52	24.10±3.50	0.036	27.91 ±1.83	22.46±2.22	0.180

Abbreviation: aGvHD, acute graft versus host disease; CR1, the first complete remission; CR2, the second complete remission; HLA, human leukemia antigen; allo-HSCT, allogeneic hematopoietic stem cell transplantation; RIC, reduced intensity

conditioning; MAC, myeloablative conditioning. GRS, GvHD- risk score; OS, overall survival; NRM, relapse-free mortality

Supplemental Table S5. Effect of potential risk factors on overall survival

Variable	Univariate analysis			Multivariate analysis*		
	HR	95% CI	*P*	HR	95% CI	*P*
age, y	1.000	0.968-1.033	0.986			
sex, male vs. female	0.619	0.288-1.333	0.220			
diagnosis, AML vs. ALL vs. MDS vs. CML	1.456	0.962-2.204	0.075			
disease status, CR vs. NR	1.187	0.731-1.930	0.488			
donor type, HLA-matched related vs. HLA-matched unrelated	2.363	1.127-4.957	0.023	2.379	1.132-4.999	0.022
donor age, y	1.030	0.995-1.067	0.094			
donor sex, male vs. female	0.694	0.296-1.624	0.399			
ABO, matched vs. mismatched	0.545	0.260-1.141	0.108			
conditioning regimen, MAC vs. RIC	1.102	0.420-2.892	0.844			
MNC, x 10^8/Kg	0.956	0.805-1.134	0.602			
CD34, x 10^6/Kg	0.864	0.726-1.028	0.099			
GRS, <-4.74 vs. ≥-4.74	2.680	1.219-5.895	0.014	2.696	1.224-5.939	0.014

Abbreviation: HR, hazard ratio; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; MDS, myelodysplastic syndrome; CML, chronic myeloid leukemia; CR, complete remission; NR, non-remission; HLA, human lymphocyte antigen; MAC, myeloablative conditioning; RIC, reduced intensity conditioning; MNC, mononuclear cells; GRS, aGvHD risk score.

* Variables with p value <.05 in univariate analysis were entered into the multivariate models onstructed by cox proportional hazards regression model.

Supplemental Table S6. ROC for GPLs enzyme surrogate genes

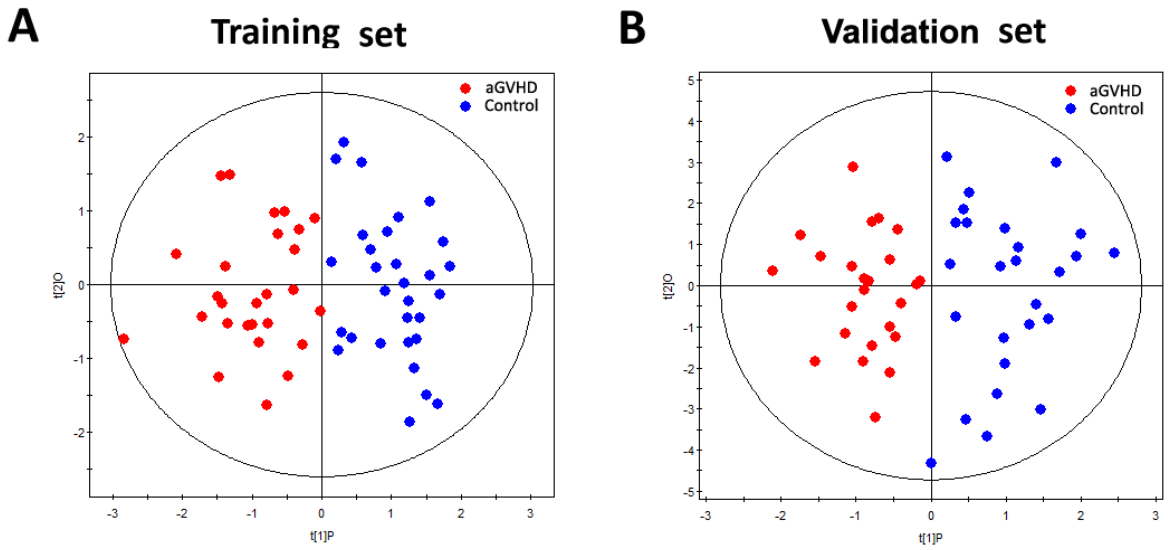
Genes	Training set			Validation set		
	P	AUC	95%CI	*P*	AUC	95%CI
LCAT	0.022	0.769	0.575-0.963	0.005	0.840	0.681-0.999
LPCAT1	0.030	0.756	0.563-0.950	0.002	0.744	0.556-1.000
LPCAT4	0.006	0.827	0.666-0.987	0.005	0.837	0.664-1.000
CHKA	0.0002	0.942	0.857-1.000	0.001	0.910	0.794-1.000
DGKE	0.007	0.821	0.656-0.985	0.0002	0.851	0.674-1.000
LPIN1	0.001	0.891	0.766-1.000	0.003	0.854	0.685-1.000
PLA2G16	0.002	0.872	0.730-1.000	0.001	0.896	0.766-1.000
PLCG1	0.002	0.865	0.719-1.000	0.007	0.826	0.653-0.999

Supplemental Table S7. The primers for qRT- PCR in the study

primer	sequence
LCAT-F	5'-CTTCACCATCTGGCTGGATCT-3'
LCAT-R	5'-AGCTTGCTGCTGTCCAGGTA-3'
LPCAT1-F	5'-AAGATGTACGGAGCGCAAGA-3'
LPCAT1-R	5'-GAATAGGTCGGTCACGGTGAG-3'
LPCAT4-F	5'-CCACCCTCTATGCCAACAAT-3'
LPCAT4-R	5'-TTCCAACGCCACCTTCAG-3'
CHKA-F	5'-CGAGGACGAGTTCCACATCA-3'
CHKA-R	5'-ATACAGCCGCAGGAGCACTT-3'
DGKE-F	5'-TCTGTTGGACCTGATGCTCTC-3'
DGKE-R	5'-CTCGCTCACCATCCAGTTCT-3'
LPIN1-F	5'-AACGAAGCCGACATCTTGGT-3'
LPIN1-R	5'-CCGTTGTCGCTTGCATGTT-3'
PLA2G16-F	5'-ACAAGGCCATCGTGAAGAAG-3'
PLA2G16-R	5'-ACTCCATAGCGCAGCTCATT-3'
PLCG1-F	5'-GACATCACCTACGGGCAGTT-3'
PLCG1-R	5'-GGAGGAAGCTGAGCATGAAC-3'
U6-homo-F	5'-AATCTAGCTGCTGCGGTTCC-3'
U6-homo-R	5'-TTCTCACGCCGGTATTCGTC-3'

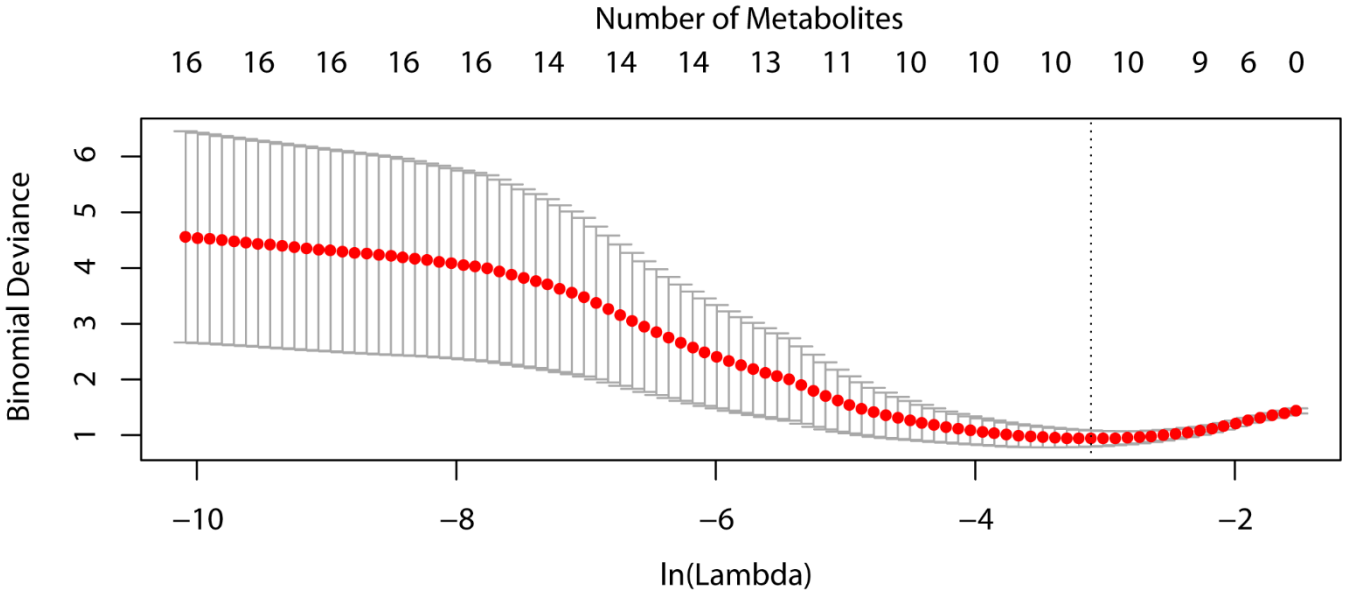
Supplemental Figures

Supplemental Figure S1.



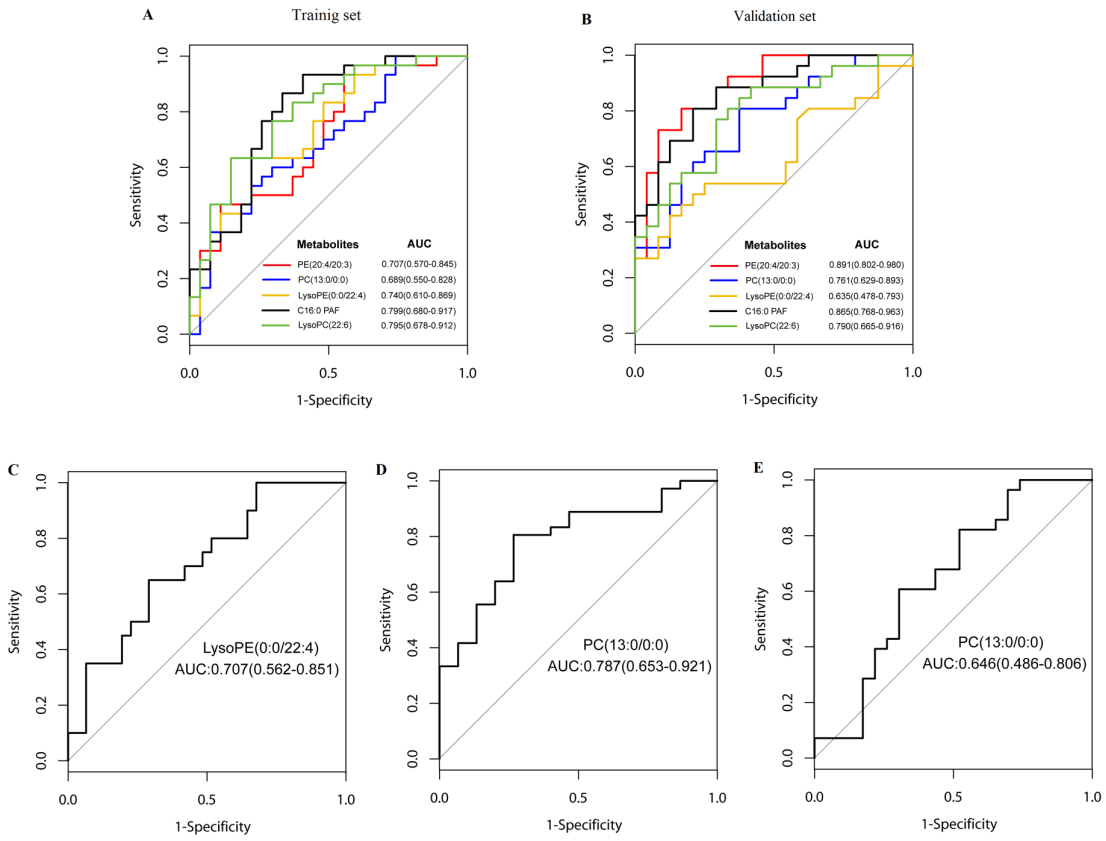
Supplemental Figure S1. OPLS-DA score plots showed a global metabolic difference between aGvHD and non-aGvHD in the training set (A) and validation set (B) at +15d after alloHSCT. A: R^2Xcum= 0.523; R^2Ycum= 0.745， Q^2cum= 0.634; B: R^2Xcum=0.519; R^2Ycum=0.684; and Q^2cum=0.576. n=57 for the training set, n=50 for the validation set.

Supplemental Figure S2.



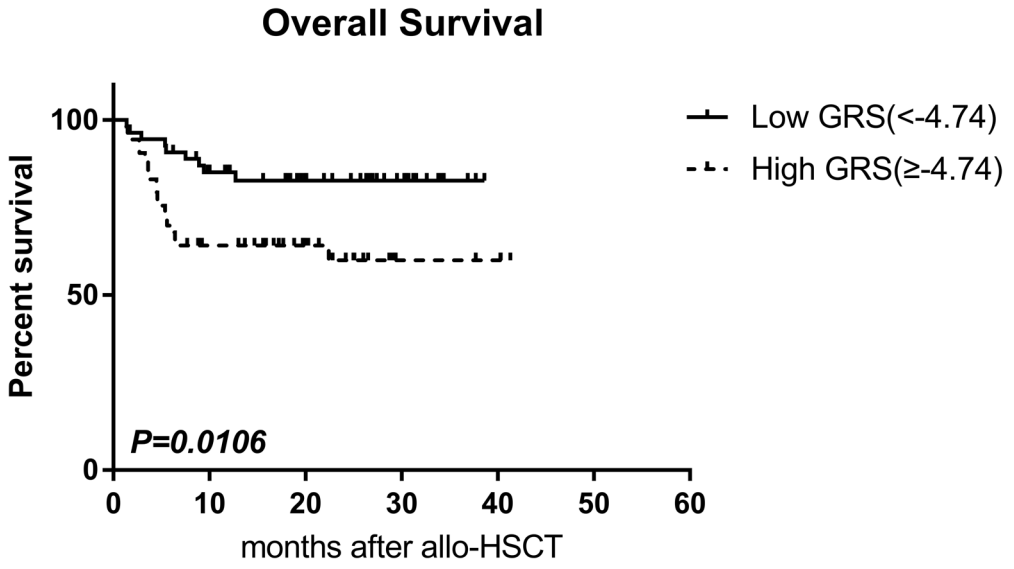
Supplemental Figure S2. Cross-validation for tuning parameter selection in the LASSO model. The solid vertical lines are binomial deviance ± standard error (SE). The dotted vertical lines are drawn at a value ln (λ) = -3.11 with the minimal model error including 10 metabolites. We chose a concise model at the accepted model errors. Herein, a value of ln (λ) = -1.71 was chosen including 5 metabolites.

Supplemental Figure S3.



Supplemental Figure S3. ROC curve analysis of the ability of different metabolites to predict aGvHD and organ specificity in patients with aGvHD. ROC curve analysis of the ability of plasma metabolites C16:0 PAF, LysoPC (22:6), PE (20:4/20:3), PC (13:0/0:0), and LysoPE (0:0/22:4) to predict the development of aGvHD based on both the training **(A)** and validation sets **(B)**, respectively. **(C)** Predictive power of 0.707 (95%CI, 0.562- 0.851) for LysoPE(0:0/22:4) that was positively correlated with liver**.** PC (13:0/0:0) was positively correlated with to skin with a predictive power of 0.787 (0.653- 0.921) **(D)** and negatively correlated with to gastrointestine with a predictive power of 0.646 (95%CI, 0.486-0.806) **(E)**.

Supplemental Figure S4.



Supplemental Figure S4. Association of the GRS with overall survival (OS) in alloHSCT recipients. Patients in high GRS group (≥-4.74, n=53) had poor overall survival (OS) compared with those in low GRS group (＜-4.74, n=54) (27.16±2.50months versus 33.00±1.71 months, P=0.0106).