

2

[illegible]

No	165	(59.78)	98	(71.01)	0.853	67	(48.55)	0.053
Yes	106	(38.41)	40	(28.99)		66	(47.83)	
Missing	5	(1.81)				5	(3.62)	
Family history								
Negative	111	(40.22)	34	(24.64)	0.818	77	(50.73)	0.861
Positive	159	(57.61)	104	(75.36)		55	(39.86)	
Missing	6	(2.17)				6	(4.35)	
BMI(median [IQR]), kg/m2								
		[15.9, 33.66]		22.40 [15.9, 32.8]			22.89 [17.01, 33.66]	
BMI stage								
Low (BIM<18.5)	16	(5.80)	14	(10.15)	0.011	2	(1.45)	0.46
Normal (BIM18.5~24.9)	92	(33.33)	83	(60.15)		9	(6.52)	
High (BIM≥25)	38	(13.77)	33	(23.91)		5	(3.62)	
Missing	130	(47.10)	8	(27.54)		122	(88.41)	
Blood group								
A	55	(19.93)	29	(21.01)	0.272	26	(18.84)	0.845
B	80	(28.99)	44	(31.88)		36	(26.09)	
AB	23	(8.33)	15	(10.87)		8	(5.80)	
O	68	(24.64)	42	(30.44)		26	(18.84)	
Missing	50	(18.12)	8	(5.80)		42	(30.44)	
Degree of differentiation								
Well-differentiated	6	(2.17)	3	(2.17)	0.518	3	(2.17)	0.133
Moderately differentiated	129	(46.74)	51	(36.96)		78	(56.52)	

Poorly differentiated	127	(46.01)	74	(53.62)		53	(38.41)	
Missing	14	(5.07)	10	(7.25)		4	(2.90)	
Lymph node metastasis								
Negative	85	(30.80)	50	(36.23)	0.149	35	(25.36)	0.002
Positive	191	(69.20)	88	(63.77)		103	(74.64)	
T stage								
T1	14	(5.07)	12	(8.70)	0.376	2	(1.45)	0.291
T2	30	(10.87)	16	(11.59)		14	(10.15)	
T3	206	(74.64)	91	(65.94)		115	(83.33)	
T4	25	(9.01)	19	(13.77)		6	(4.35)	
Missing	1	(0.36)	0	(0.00)		1	(0.73)	
TNM stage								
I	12	(4.35)	12	(8.70)	0.501	0	(0.00)	0.001
II	82	(29.71)	44	(31.88)		38	(27.54)	
III	162	(58.70)	63	(45.65)		99	(71.74)	
IV	19	(6.88)	19	(13.77)		0	(0.00)	
Missing	1	(0.36)	0	(0.00)		1	(0.73)	

3 *High/Low incidence area: The areas with a mortality rate of more than 60/100,000 are high incidence areas, and the mortality rate low
4 than 60/100,000 are low incidence areas.

5 Table 2. 25 differential metabolites including to 11 up-regulated and 14 down-regulated metabolites were significantly altered in the
6 discovery and validationsets

Compounds	Discovery set		Validation set		Type
	<i>p</i> -value	FC	<i>p</i> -value	FC	
4-Guanidinobutyric Acid	0.00	1.28	0.00	1.57	UP
12,13-DiHOME	0.00	0.75	0.00	0.71	DOWN
Aldosterone	0.00	0.68	0.00	0.68	DOWN
N1-Acetylspermine	0.00	2.33	0.00	1.42	UP
3-Indolepropionic Acid	0.01	0.16	0.00	0.38	DOWN
Acetylcholine	0.00	1.35	0.00	1.55	UP
All-Trans-13,14-Dihydroretinol	0.00	1.46	0.00	2.10	UP
L-2-Aminobutyric acid	0.00	1.34	0.00	1.47	UP
Glycochenodeoxycholic Acid	0.00	0.38	0.00	0.33	DOWN
L-Proline	0.00	0.80	0.00	0.68	DOWN
Glycine deoxycholic acid	0.00	0.35	0.00	0.36	DOWN
Trans-3-Hydroxycotinine	0.01	0.18	0.00	0.06	DOWN
Prostaglandin E2	0.00	0.22	0.00	0.08	DOWN
7-ketolithocholic acid	0.00	0.29	0.00	0.28	DOWN
12-ketolithocholic acid	0.00	0.29	0.00	0.28	DOWN
Hododeoxycholic acid	0.00	0.27	0.00	0.17	DOWN
2-Hydroxybutanoic Acid	0.00	2.01	0.00	2.56	UP

L-Histidine	0.00	0.79	0.00	0.69	DOWN
Capric Acid(C10:0)	0.00	3.18	0.00	1.36	UP
Sphingosine	0.00	0.71	0.00	0.63	DOWN
4-Hydroxytryptamine	0.01	0.26	0.00	0.08	DOWN
4-Pyridoxic Acid	0.00	9.49	0.00	2.28	UP
L-Fucose	0.00	3.30	0.00	1.86	UP
Malonic acid	0.00	4.03	0.00	2.00	UP
3-Hydroxybutyrate	0.00	4.04	0.00	1.99	UP

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Table S1. 200 differential metabolites altered in the 2 sets

Compounds	Discovery set		Validation set		Type	Classification of metabolites	
	<i>p</i> -value	FC	<i>p</i> -value	FC		Class I	Class II
Carnitine C22:2	0.00	0.74	0.00	0.51	DOWN	*FA	*CAR
PE (18: 1 (9Z) / 0: 0)	0.00	0.72	0.00	0.69	DOWN	*GP	*PE
Lysope 18:1	0.00	0.71	0.00	0.61	DOWN	GP	*LPE
Marmesin	0.00	0.74	0.00	0.60	DOWN	Aldehyde,Ketones,Esters	Esters
2-Methyl-4-pentenoic Acid	0.00	9.36	0.00	90.29	UP	Organic acid and its derivatives	Organic acid and its derivatives
4-Acetamidobutyric Acid	0.00	1.30	0.00	1.51	UP	Organic acid and its derivatives	Organic acid and its derivatives
2-Linoleoyl Glycerol	0.00	1.65	0.00	1.64	UP	*GL	*MG
2-Hydroxy-2-(4-hydroxy-3-methoxyphenyl)acetic acid	0.00	0.57	0.00	0.73	DOWN	Benzene and substituted derivatives	Phenolic acids
Glycocholic Acid	0.00	0.55	0.00	0.48	DOWN	Bile acids	Bile acids
N-Acetylmethionine	0.00	1.60	0.00	4.23	UP	Amino acid and its metabolomics	Amino acid derivatives
Carnitine C8-OH	0.00	0.73	0.00	0.41	DOWN	FA	CAR
3-Hydroxy-3-Methyl Butyric acid	0.00	1.32	0.00	1.65	UP	Organic acid and its derivatives	Organic acid and its derivatives
trans-3-Indoleacrylic acid	0.00	0.27	0.00	0.40	DOWN	Organic acid and its derivatives	Organic acid and its derivatives

3'-Sialyllactose	0.00	1.29	0.00	2.32	UP	Carboxylic acids and derivatives	Sugars
Lysopc 18:0	0.00	0.76	0.00	0.71	DOWN	*GP	*LPC
PAF C-16	0.00	0.76	0.00	0.71	DOWN	GP	LPC
5-Hydroxyindole-3-Acetic Acid	0.00	0.51	0.00	0.36	DOWN	Heterocyclic compounds	Indole and its derivatives
Di-n-propyl phthalate	0.00	0.49	0.00	0.69	DOWN	Aldehyde,Ketones,Esters	Esters
4-Guanidinobutyric Acid	0.00	1.28	0.00	1.57	UP	Organic acid and its derivatives	Organic acid and its derivatives
Formononetin	0.00	0.49	0.00	0.69	DOWN	Benzene and substituted derivatives	Benzene and substituted derivatives
9,10-DiHOME							
[(±)9,10-dihydroxy-12Z-octadecenoic acid]	0.00	0.75	0.00	0.71	DOWN	Oxidized lipids	Oxidized lipids
12,13-DiHOME	0.00	0.75	0.00	0.71	DOWN	Oxidized lipids	Oxidized lipids
Aldosterone	0.00	0.68	0.00	0.68	DOWN	Aldehyde,Ketones,Esters	Ketones
N1-Acetylspermine	0.00	2.33	0.00	1.42	UP	Organic acid and its derivatives	Organic acid and its derivatives
LysoPC 18:0(2n isomer)	0.00	0.75	0.00	0.71	DOWN	GP	LPC
3-Indolepropionic Acid	0.01	0.16	0.00	0.38	DOWN	Heterocyclic compounds	Indole and its derivatives
Carnitine C10:1	0.00	0.47	0.00	0.45	DOWN	FA	CAR
N-Methyltryptamine	0.00	0.41	0.00	0.40	DOWN	Tryptamines,Cholines,Pigments	Tryptamines
Acetylcholine	0.00	1.35	0.00	1.55	UP	Alcohol and amines	Polyamines
3-Carboxypropyltrimethyl	0.00	1.35	0.00	1.55	UP	Organic acid and its derivatives	Organic acid and its derivatives

ammonium							
MG(20:4)isomer	0.00	1.49	0.00	2.46	UP	*GL	*MG
Alpha-Mercholic Acid	0.00	0.45	0.00	0.34	DOWN	Bile acids	Bile acids
Sn-Glycero-3-phosphochol ine	0.00	0.66	0.00	0.61	DOWN	Tryptamines,Cholines,Pigments	Cholines
Carnitine C15:1:DC	0.00	0.36	0.00	0.21	DOWN	FA	CAR
Lysope 14:0	0.00	0.48	0.00	0.48	DOWN	GP	LPE
Glycoursodeoxycholic acid	0.00	0.38	0.00	0.19	DOWN	Bile acids	Bile acids
tryptophan betaine	0.00	0.52	0.00	0.30	DOWN	Organic acid and its derivatives	Organic acid and its derivatives
Carnitine C16:2	0.00	0.79	0.00	0.74	DOWN	FA	CAR
Theobromine	0.03	0.24	0.00	0.15	DOWN	Nucleotide and its metabolomics	Nucleotide and its metabolomics
Carnitine C16:2 Isomer1	0.00	0.79	0.00	0.73	DOWN	FA	CAR
9-HpODE	0.00	0.48	0.00	0.68	DOWN	Oxidized lipids	Oxidized lipids
Carnitine C14:2 Isomer 1	0.00	0.52	0.00	0.40	DOWN	FA	CAR
All-Trans-13,14-Dihydror etinol	0.00	1.46	0.00	2.10	UP	CoEnzyme and vitamins	CoEnzyme and vitamins
Glycohyodeoxycholic acid	0.00	0.37	0.00	0.18	DOWN	Bile acids	Bile acids
L-2-Aminobutyric acid	0.00	1.34	0.00	1.47	UP	Organic acid and its derivatives	Organic acid and its derivatives
Delta-Hexalactone	0.00	1.59	0.00	127.4 0	UP	Aldehyde,Ketones,Esters	Esters

MG(22:6)isomer	0.00	2.00	0.00	2.24	UP		GL	MG
MG(22:6)	0.00	2.00	0.00	2.24	UP		GL	MG
Lysopa 18:0	0.00	0.67	0.00	0.66	DOWN		*GP	LPC
1-Methylxanthine	0.00	0.52	0.00	0.34	DOWN	Nucleotide and its metabolomics	Nucleotide and its metabolomics	
Cis-9,10-epoxystearic acid	0.00	0.77	0.00	0.46	DOWN		FA	*FFA
16-Hydroxyhexadecanoic acid	0.00	0.65	0.00	0.29	DOWN		FA	FFA
Lysope 18:0	0.00	0.70	0.00	0.73	DOWN		GP	*LPE
PysoPE 18:0(2n isomer)	0.00	0.70	0.00	0.73	DOWN		GP	LPE
Urobilin	0.05	1.47	0.00	2.49	UP	Tryptamines,Cholines,Pigments		Pigments
L-Cysteine	0.00	0.52	0.00	0.37	DOWN	Amino acid and Its metabolomics		Amino acids
12,13-EpOME								
[(±)12(13)epoxy-9Z-octadecenoic acid]	0.00	0.62	0.00	0.46	DOWN		Oxidized lipids	Oxidized lipids
9,10-EpOME								
[(±)9,10-epoxy-12Z-octadecenoic acid]	0.00	0.62	0.00	0.46	DOWN		Oxidized lipids	Oxidized lipids
N-arachidene glycine	0.00	1.41	0.00	1.99	UP	Aldehyde,Ketones,Esters		Esters
Carnitine C14:2	0.00	0.67	0.00	0.59	DOWN		FA	CAR

Carnitine C9:0	0.00	0.32	0.00	0.25	DOWN	FA	CAR
Lysopc 18:2	0.00	0.76	0.00	0.69	DOWN	GP	LPC
Lysopc 18:2 (2N Isomer)	0.00	0.76	0.00	0.69	DOWN	GP	LPE
Dopaquinone	0.00	0.40	0.00	0.42	DOWN	Benzene and substituted derivatives	Benzene and substituted derivatives
Trigonelline	0.00	0.56	0.00	0.56	DOWN	CoEnzyme and vitamins	Co-Enzyme and vitamins
3-Methylcrotonyl Glycine	0.00	0.60	0.00	0.50	DOWN	Organic acid and its derivatives	Organic acid and its derivatives
Trimethylamine N-Oxide	0.00	0.66	0.00	0.50	DOWN	Alcohol and amines	Amines
1-Aminopropan-2-ol	0.00	0.66	0.00	0.50	DOWN	Alcohol and amines	Alcohols
Carnitine C16:2-OH	0.00	0.78	0.00	0.58	DOWN	FA	CAR
D-Sorbitol	0.00	8.72	0.00	1.34	UP	Carboxylic acids and derivatives	Sugar alcohols
2-Methoxy-4-[(E)-prop-1-enyl]phenol	0.00	83.73	0.00	123.32	UP	Benzene and substituted derivatives	Benzene and substituted derivatives
5-iPF2 α -VI							
[(8 β)-5,9 α ,11 α -trihydroxy-prosta-6E,14Z-dien-1-oic acid]	0.00	11383.38	0.00	3.04	UP	Oxidized lipids	Oxidized lipids
Carnitine C14:2-OH	0.00	0.78	0.00	0.58	DOWN	FA	CAR
Phe-Met	0.00	0.78	0.00	0.09	DOWN	Amino acid and its metabolomics	Small Peptide
Lysopc 14:0	0.00	0.48	0.00	0.43	DOWN	GP	LPC

Dulcitol	0.00	6.72	0.00	1.99	UP	Carboxylic acids and derivatives	Sugar alcohols
8-Epidermal glycoside	0.00	0.78	0.00	0.77	DOWN	Others	Others
Lysopc 17:0	0.00	0.66	0.00	0.63	DOWN	GP	LPC
(±)12-HEPE							
[(±)-12-hydroxy-5Z,8Z,10E,14Z,17Z-eicosapentaenoic acid]	0.00	0.70	0.00	0.35	DOWN	Oxidized lipids	Oxidized lipids
(±)15-HEPE							
[(±)-15-hydroxy-5Z,8Z,11Z,13E,17Z-eicosapentaenoic acid]	0.00	0.70	0.00	0.35	DOWN	Oxidized lipids	Oxidized lipids
(±)18-HEPE							
[(±)-18-hydroxy-5Z,8Z,11Z,14Z,16E-eicosapentaenoic acid]	0.00	0.70	0.00	0.35	DOWN	Oxidized lipids	Oxidized lipids
Acetyl Tryptophan	0.00	0.71	0.00	0.43	DOWN	Amino acid and its metabolomics	Amino acid derivatives
3,3',5-Triiodo-L-Thyronine	0.00	0.74	0.00	0.49	DOWN	Hormones and hormone related compounds	Hormones and hormone related compounds
2-Hydroxycaprylic acid	0.00	0.62	0.00	0.45	DOWN	Organic acid and its derivatives	Organic acid and its derivatives
Butenoyl PAF	0.00	0.75	0.00	0.69	DOWN	Others	Others

Maleic Acid	0.00	0.80	0.00	0.69	DOWN	Organic acid and its derivatives	Organic acid and its derivatives
PysoPE 18:2	0.00	0.66	0.00	0.55	DOWN	GP	LPE
Lysopg 18:1	0.00	0.69	0.00	0.68	DOWN	GP	LPG
Glycochenodeoxycholic Acid	0.00	0.38	0.00	0.33	DOWN	Bile acids	Bile acids
DI-2-Aminooctanoic Acid	0.01	0.69	0.00	0.35	DOWN	Organic acid and its derivatives	Organic acid and its derivatives
L-Proline	0.00	0.80	0.00	0.68	DOWN	Amino acid and its metabolomics	Amino acids
LysoPC 18:2(2n isomer1)	0.00	0.76	0.00	0.70	DOWN	GP	LPC
N α -Acetyl-L-Arginine	0.00	0.69	0.00	0.67	DOWN	Amino acid and its metabolomics	Amino acid derivatives
Carnitine C10:1 Isomer1	0.00	0.39	0.00	0.45	DOWN	FA	CAR
3-Hydroxyhippuric Acid	0.00	0.36	0.00	0.40	DOWN	Amino acid and its metabolomics	Amino acid derivatives
4-Hydroxyhippurate	0.00	0.36	0.00	0.38	DOWN	Amino acid and its metabolomics	Amino acid derivatives
Hydrocinnamic Acid	0.00	0.33	0.00	0.30	DOWN	Organic acid and its derivatives	Organic acid and its derivatives
LysoPC 20:1(2n isomer)	0.00	0.77	0.00	0.68	DOWN	GP	LPC
Lysopc 20:1	0.00	0.75	0.00	0.69	DOWN	GP	LPC
Piperidone	0.00	1.32	0.00	1.43	UP	Heterocyclic compounds	Heterocyclic compounds
Glycine deoxycholic acid	0.00	0.35	0.00	0.36	DOWN	Bile acids	Bile acids

D-Mannitol	0.00	11.23	0.00	1.47	UP	Carboxylic acids and derivatives	Sugar alcohols
Carnitine C18:4	0.00	0.78	0.00	0.70	DOWN	FA	CAR
Lysopa 16:0	0.00	0.77	0.00	0.76	DOWN	GP	LPC
Trans-3-Hydroxycotinine	0.01	0.18	0.00	0.06	DOWN	Heterocyclic compounds	Heterocyclic compounds
Carnitine C12:1	0.00	0.62	0.00	0.51	DOWN	FA	CAR
2-Hydroxy HippuricAcid	0.00	0.39	0.00	0.00	DOWN	Benzene and substituted derivatives	Phenolic acids
Dodecylcarnitine	0.00	0.55	0.00	0.39	DOWN	FA	CAR
3-(3-Hydroxyphenyl)Propionate Acid	0.00	0.17	0.00	0.22	DOWN	Organic acid and its derivatives	Organic acid and its derivatives
3-(4-Hydroxyphenyl)-Propionic Acid	0.00	0.17	0.00	0.22	DOWN	Benzene and substituted derivatives	Phenolic acids
Carnitine C10:0	0.00	0.52	0.00	0.36	DOWN	FA	CAR
LysoPC 16:1(2n isomer)	0.00	0.71	0.00	0.55	DOWN	GP	LPC
Carnitine C8:0	0.00	0.50	0.00	0.43	DOWN	FA	CAR
Carnitine C16:3	0.00	0.68	0.01	0.73	DOWN	FA	CAR
Phe-Asn	0.01	0.73	0.00	0.32	DOWN	Amino acid and Its metabolomics	Small Peptide
Lysope 16:0	0.00	0.76	0.00	0.60	DOWN	GP	LPE
PysoPE 16:0(2n isomer)	0.00	0.76	0.00	0.60	DOWN	GP	LPE
Lysops 22:6	0.00	0.66	0.00	0.73	DOWN	GP	LPS

Taurodeoxycholic acid	0.00	0.48	0.00	0.28	DOWN	Bile acids	Bile acids
23-deoxydeoxycholic acid	0.00	0.41	0.00	0.41	DOWN	Bile acids	Bile acids
Glutamine	0.00	0.73	0.00	0.56	DOWN	Amino acid and Its metabolomics	Amino acids
(4Z, 7Z, 10Z, 13Z, 16Z, 19Z) -Eicosaheenoate	0.00	0.24	0.00	0.19	DOWN	Aldehyde,Ketones,Esters	Esters
Methanesulfonic acid	0.00	0.58	0.00	0.58	DOWN	Organic acid and its derivatives	Sulfonic acids
Gamma-Mercholic Acid	0.00	0.27	0.00	0.17	DOWN	Bile acids	Bile acids
Prostaglandin E2	0.00	0.22	0.00	0.08	DOWN	Hormones and hormone related compounds	Hormones and hormone related compounds
6-hydroxy-3-succinylpyrid ine	0.00	0.33	0.00	0.38	DOWN	Heterocyclic compounds	Heterocyclic compounds
(±) -Myristylcarnitine	0.00	0.80	0.00	0.66	DOWN	FA	CAR
Pregnanetriol	0.00	0.70	0.00	0.45	DOWN	Alcohol and amines	Alcohols
N-Acetylphenylalanine	0.00	0.78	0.00	0.77	DOWN	Amino acid and Its metabolomics	Amino acid derivatives
Lysopc 15:0	0.00	0.71	0.00	0.61	DOWN	GP	LPC
PysoPE 20:5(2n isomer1)	0.00	0.55	0.00	0.70	DOWN	GP	LPE
PysoPE 20:5	0.00	0.55	0.00	0.70	DOWN	GP	LPE
Decanoyl L-Carnitine	0.00	0.51	0.00	0.36	DOWN	FA	CAR
Carnitine C14:0	0.00	0.79	0.00	0.66	DOWN	FA	CAR

8,8a-deoxy oleanoic acid	0.00	0.27	0.00	0.18	DOWN	Others	Others
MG (18: 2 (9Z, 12Z) / 0: 0/0: 0) [rac]	0.00	0.70	0.00	0.45	DOWN	GL	MG
11-Cis-Retinol	0.00	0.66	0.00	0.53	DOWN	CoEnzyme and vitamins	CoEnzyme and vitamins
7-Ketolithocholic acid	0.00	0.29	0.00	0.28	DOWN	Bile acids	Bile acids
12-Ketolithocholic acid	0.00	0.29	0.00	0.28	DOWN	Bile acids	Bile acids
Hododeoxycholic acid	0.00	0.27	0.00	0.17	DOWN	Bile acids	Bile acids
Carnitine C7:1 Isomer1	0.00	0.35	0.00	0.40	DOWN	FA	CAR
Carnitine C13:0	0.01	0.75	0.00	0.40	DOWN	FA	CAR
Lysophosphatidylcholine 16:1	0.00	0.76	0.00	0.54	DOWN	GP	LPC
Carnitine C14:3	0.00	0.57	0.00	0.61	DOWN	FA	CAR
3-(Pyrazol-1-yl) -L-alanine	0.00	0.78	0.00	0.72	DOWN	Amino acid and Its metabolomics	Amino acid derivatives
Cholesterol	0.00	0.42	0.00	0.34	DOWN	Hormones and hormone related compounds	Hormones and hormone related compounds
Carnitine C10:0 Isomer1	0.00	0.50	0.00	0.36	DOWN	FA	CAR
Testosterone	0.00	0.69	0.00	0.17	DOWN	Hormones and hormone related compounds	Hormones and hormone related compounds
Carnitine C7:1	0.00	0.33	0.00	0.42	DOWN	FA	CAR
Salicylaldehyde	0.00	0.19	0.00	0.18	DOWN	Benzene and substituted derivatives	Benzene and substituted derivatives

Carnitine C11:0	0.00	0.50	0.00	0.23	DOWN	FA	CAR
Carnitine C13:1	0.00	0.52	0.00	0.41	DOWN	FA	CAR
Indole-5-carboxylic acid	0.00	0.74	0.00	0.50	DOWN	Heterocyclic compounds	Indole and its derivatives
LysoPE(16:1(9Z)/0:0)	0.00	0.69	0.00	0.40	DOWN	GP	LPE
2-Hydroxybutanoic Acid	0.00	2.01	0.00	2.56	UP	Organic acid and its derivatives	Organic acid and its derivatives
Carnitine ph-C1	0.00	0.35	0.00	0.30	DOWN	FA	CAR
Carnitine C13:0 Isomer1	0.00	0.64	0.00	0.40	DOWN	FA	CAR
L-Histidine	0.00	0.79	0.00	0.69	DOWN	Amino acid and Its metabolomics	Amino acids
Carnitine C9:0 Isomer1	0.00	0.51	0.00	0.29	DOWN	FA	CAR
Capric Acid(C10:0)	0.00	3.18	0.00	1.36	UP	FA	FFA
Caffeic Acid	0.00	0.18	0.00	0.17	DOWN	Organic acid and its derivatives	Organic acid and its derivatives
PysoPE 16:1	0.00	0.69	0.00	0.37	DOWN	GP	LPE
9,12-Octadecadienoic acid	0.00	0.72	0.00	0.56	DOWN	FA	FFA
Carnitine C7:0	0.00	0.68	0.00	0.43	DOWN	FA	CAR
LysoPC 20:3(2n isomer)	0.00	0.74	0.00	0.69	DOWN	GP	LPC
LysoPC 20:3	0.00	0.74	0.00	0.69	DOWN	GP	LPC
Carnitine C11:1	0.00	0.62	0.00	0.49	DOWN	FA	CAR
Stearidonic Acid	0.00	0.73	0.00	0.62	DOWN	FA	FFA
Styrene	0.00	0.19	0.00	0.19	DOWN	Benzene and substituted derivatives	Benzene and substituted derivatives

Lysopc 20:2	0.00	0.66	0.00	0.77	DOWN	GP	LPC
Lithocholic acid	0.00	0.35	0.00	0.21	DOWN	Bile acids	Bile acids
19(S)-HETE							
[19S-hydroxy-5Z,8Z,11Z, 14Z-eicosatetraenoic acid]	0.00	1.55	0.00	2.82	UP	Oxidized lipids	Oxidized lipids
20-HETE							
[20-Hydroxy-5Z,8Z,11Z,1 4Z-eicosatetraenoic acid]	0.00	1.55	0.00	2.82	UP	Oxidized lipids	Oxidized lipids
Carnitine C10:1-OH	0.00	0.29	0.00	0.31	DOWN	FA	CAR
Phe-Phe	0.00	0.69	0.00	0.39	DOWN	Amino acid and Its metabolomics	Small peptide
Sphingosine	0.00	0.71	0.00	0.63	DOWN	SL	SM
Hippuric Acid	0.00	0.18	0.00	0.17	DOWN	Organic acid and its derivatives	Organic acid and its derivatives
7-Ketodeoxycholic acid	0.00	0.35	0.01	0.47	DOWN	Hormones and hormone related compounds	Hormones and hormone related compounds
L-Citrulline	0.00	0.70	0.00	0.61	DOWN	Amino acid and Its metabolomics	Amino acids
Cyclohexylamine	0.01	0.69	0.00	0.40	DOWN	Alcohol and amines	Amines
Urocanic Acid	0.00	1.35	0.00	1.86	UP	Organic acid and its derivatives	Organic acid and its derivatives
1,2-Dodecanoyl PC	0.00	0.74	0.00	0.65	DOWN	GP	PC
1,2-Epoxy-3-(p-nitropheno	0.00	0.72	0.00	0.01	DOWN	Benzene and substituted	Benzene and substituted

xy) propane						derivatives	derivatives
2-(Formylamino)Benzoic Acid	0.00	0.55	0.00	0.54	DOWN	Benzene and substituted derivatives	Phenolic acids
4-Hydroxytryptamine	0.01	0.26	0.00	0.08	DOWN	Tryptamines, Cholines, Pigments	Tryptamines
PysoPE 22:4(2n isomer1)	0.00	0.72	0.00	0.51	DOWN	GP	LPE
PysoPE 22:4	0.00	0.72	0.00	0.51	DOWN	GP	LPE
PysoPE 20:3(2n isomer1)	0.00	0.59	0.00	0.44	DOWN	GP	LPE
PysoPE 20:3	0.00	0.59	0.00	0.44	DOWN	GP	LPE
LysoPC 20:2(2n isomer2)	0.00	0.66	0.00	0.76	DOWN	GP	LPC
LysoPC 20:2(2n isomer1)	0.00	0.66	0.00	0.76	DOWN	GP	LPC
Orthocholic acid	0.00	0.20	0.00	0.27	DOWN	Bile acids	Bile acids
RvE1							
[5S,12R,18R-trihydroxy-6Z,8E,10E,14Z,16E-eicosapentaenoic acid]	0.00	0.57	0.00	0.04	DOWN	Oxidized lipids	Oxidized lipids
4-Pyridoxic Acid	0.00	9.49	0.00	2.28	UP	Heterocyclic compounds	Pyridine and pyridine derivatives
Carnitine C9:1	0.00	0.36	0.00	0.37	DOWN	FA	CAR
δ-Valerolactam	0.01	0.69	0.00	0.37	DOWN	Alcohol and amines	Amines
L-Fucose	0.00	3.30	0.00	1.86	UP	Carboxylic acids and derivatives	Sugars

L-Rhamnose	0.00	3.30	0.00	1.86	UP	Carboxylic acids and derivatives	Sugars
Malonic acid	0.00	4.03	0.00	2.00	UP	Organic acid and its derivatives	Organic acid and its derivatives
3-Hydroxybutyrate	0.00	4.04	0.00	1.99	UP	Organic acid and its derivatives	Organic acid and its derivatives

10 *FA: Fatty Acyls;

11 CAR:Carnitine;

12 GP: Glycerophospholipids;

13 PE: Phosphatidylethanolamine;

14 LPE: Lysophosphatidylethanolamine;

15 GL:Glycerolipids;

16 MGA: Monoglyceride;

17 LPC: Lysophosphatidylcholine;

18 FFA: Free fatty acid;

19 LPG:Lysophosphatidylglycerol;

20 LPS: Lysophosphatidylserine;

21 SL: Sphingolipids;

22 SM: Sphingomyelin;

23 PC: Phosphatidylcholine;

24

25

Table S2. 200 differential metabolites altered in the 2 sets

Classification of metabolites	Count item: Class I	Classification of metabolites	Count item: Class II
Alcohol and amines	6	Alcohols	2
Aldehyde,Ketones,Esters	6	Amines	3
Amino acid and its metabolomics	15	Amino acid derivatives	7
Benzene and substituted derivatives	10	Amino acids	5
Bile acids	14	Benzene and substituted derivatives	6
Carboxylic acids and derivatives	6	Bile acids	14
CoEnzyme and vitamins	3	*CAR	35
*FA	40	Cholines	1
*GL	5	CoEnzyme and vitamins	3
*GP	39	Esters	5
Heterocyclic compounds	7	*FFA	5
Hormones and hormone related compounds	5	Heterocyclic compounds	3
Nucleotide and its metabolomics	2	Hormones and hormone related compounds	5
Organic acid and its derivatives	22	Indole and its derivatives	3
Others	3	Ketones	1
Oxidized lipids	12	*LPC	19
*SL	1	*LPE	16
Tryptamines,Cholines,Pigments	4	*LPG	1
Total	200	*LPS	1
		*MG	5
		Nucleotide and its metabolomics	2
		organic acid and its derivatives	21
		Others	3
		Oxidized lipids	12
		*PC	1
		*PE	1
		Phenolic acids	4
		Pigments	1

Polyamines	1
Pyridine and pyridine derivatives	1
SM	1
Small peptide	3
Sugar alcohols	3
Sugars	3
Sulfonic acids	1
Tryptamines	2
Total	200

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- 27 *FA: Fatty Acyls;
- 28 CAR:Carnitine;
- 29 GP: Glycerophospholipids;
- 30 PE: Phosphatidylethanolamine;
- 31 LPE: Lysophosphatidylethanolamine;
- 32 GL:Glycerolipids;
- 33 MGA: Monoglyceride;
- 34 LPC: Lysophosphatidylcholine;
- 35 FFA: Free fatty acid;
- 36 LPG:Lysophosphatidylglycerol;
- 37 LPS: Lysophosphatidylserine;
- 38 SL: Sphingolipids;
- 39 SM: Sphingomyelin;
- 40 PC: Phosphatidylcholine;
- 41
- 42