

Table S1. The biomarkers identified *via* MetaboAnalyst software between the SHR-Untreated and SHR-RVPSL groups in both positive and negative ion modes. SHR-RVPSL group vs SHR-Untreated group: $p < 0.05$, $VIP > 1$, Fold change ≥ 2 or ≤ 0.5 .

NO.	Metabolite	Formula	Trend	KEGG map
1	GANT 61	$C_{27}H_{35}N_5$	up	--
2	LY255283	$C_{19}H_{28}N_4O_3$	up	--
3	Pro Ala Asp Lys Thr	$C_{22}H_{38}N_6O_9$	up	--
4	Acetyl-L-carnitine	$C_9H_{17}NO_4$	up	ko04931
5	Choline	$C_5H_{13}NO$	up	ko00260, ko00564, ko01100, ko02010, ko04725, ko04976, ko05231
6	Phe Ala Glu Lys Ile	$C_{29}H_{46}N_6O_8$	up	--
7	Adenosine	$C_{10}H_{13}N_5O_4$	up	ko00230, ko01100, ko02010, ko04022, ko04024, ko04071, ko04080, ko04270, ko04923, ko04924, ko05012, ko05032, ko05034
8	CL(i-14:0/i-17:0/i-16:0/a-21:0) [rac]	$C_{77}H_{150}O_{17}P_2$	up	--
9	Monoethylhexyl phthalic acid	$C_{16}H_{22}O_4$	up	--
10	Anhydrotetracycline	$C_{22}H_{22}N_2O_7$	up	ko00253, ko01057, ko01100, ko01110
11	Leu Thr Gln Gln Leu	$C_{26}H_{47}N_7O_9$	up	--
12	N-Nervonoyl-D-erythro-sphingosylphosphorylcholine	$C_{47}H_{93}N_2O_6P$	up	--
13	13Z-Docosenamide	$C_{22}H_{43}NO$	up	--
14	PC (20:4(5Z,8Z,11Z,14Z)/20:4(5Z,8Z,11Z,14Z))	$C_{48}H_{80}NO_8P$	up	--
15	Linoleoyl Ethanolamide	$C_{20}H_{37}NO_2$	up	--
16	His Ile Asn	$C_{16}H_{26}N_6O_5$	up	--
17	Kalkitoxin thioamide alcohol	$C_{21}H_{40}N_2O_2S$	up	--

Table S1 (contd.)

NO.	Metabolite	Formula	Trend	KEGG map
18	1,2-dioleoyl-sn-glycero-3-phosphatidylcholine	C ₄₄ H ₈₄ NO ₈ P	up	--
19	1-O-Hexadecyl-2-O-acetyl-sn-glycerol-3-phosphorylcholine	C ₂₆ H ₅₄ NO ₇ P	up	--
20	2,5-Dimethylbenzaldehyde	C ₉ H ₁₀ O	up	--
21	(-)-11-nor-9-carboxy- 9-THC	C ₂₁ H ₂₈ O ₄	up	--
22	Leu Val Phe Ala Ile	C ₂₉ H ₄₇ N ₅ O ₆	up	--
23	Metenamine	C ₆ H ₁₂ N ₄	up	--
24	PA (22:1(13Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	C ₄₇ H ₇₉ O ₈ P	up	--
25	4-Hydroxyacid;4-Hydroxyalkanoic acid; 4-Hydroxycarboxylic acid	C ₄ H ₈ O ₃	up	--
26	1-heptadecanoyl-sn-glycero-3-phosphocholine	C ₂₅ H ₅₂ NO ₇ P	up	--
27	Adrenic Acid	C ₂₂ H ₃₆ O ₂	up	ko01040, ko04216
28	Oleyl alcohol	C ₁₈ H ₃₆ O	up	--
29	Eicosa-5Z,8Z-dienoic acid (20:2, n-12)	C ₂₀ H ₃₆ O ₂	up	--
30	Drospirenone	C ₂₄ H ₃₀ O ₃	up	--
31	Triazamate	C ₁₃ H ₂₂ N ₄ O ₃ S	up	--
32	(+)-trans-C75	C ₁₄ H ₂₂ O ₄	up	--
33	Geldanamycin Analog	C ₂₈ H ₃₉ N ₃ O ₈	up	--
34	Niacinamide	C ₆ H ₆ N ₂ O	up	ko00760, ko01100, ko04212, ko04977
35	Tetradecanedioic acid	C ₁₄ H ₂₆ O ₄	up	--
36	(+)-Tocopherol	C ₂₉ H ₅₀ O ₂	up	--
37	4-Propylphenol	C ₉ H ₁₂ O	up	--
38	Loxidine; Lavoltidine	C ₁₉ H ₂₉ N ₅ O ₂	up	--
39	13(R)-HODE	C ₁₈ H ₃₂ O ₃	up	--

Table S1 (contd.)

NO.	Metabolite	Formula	Trend	KEGG map
40	Lys Glu Thr Glu	C ₂₀ H ₃₅ N ₅ O ₁₀	up	--
41	2-N-Dodecyltetrahydrothiophene; DTHT	C ₁₆ H ₃₂ S	up	--
42	Glycocholic Acid	C ₂₆ H ₄₃ NO ₆	up	ko00120, ko00121, ko01100, ko04976, ko04979
43	1-Stearoyl-2-hydroxy-sn-glycero-3-phosphocholine	C ₂₆ H ₅₄ NO ₇ P	up	--
44	Gln Phe His	C ₂₀ H ₂₆ N ₆ O ₅	up	--
45	Asp Asp Arg	C ₁₄ H ₂₄ N ₆ O ₈	up	--
46	Isodesmosine	C ₂₄ H ₄₀ N ₅ O ₈	up	--
47	Thr Val Thr Phe Tyr	C ₃₁ H ₄₃ N ₅ O ₉	up	--
48	Minosaminomycin	C ₂₅ H ₄₆ N ₈ O ₁₀	up	--
49	Oxyphenyclimine	C ₂₀ H ₂₈ N ₂ O ₃	up	--
50	Tyr Arg Phe	C ₂₄ H ₃₂ N ₆ O ₅	up	--
51	3alpha,7alpha,12alpha-Trihydroxy-5alpha-cholan-24-oic acid	C ₂₄ H ₄₀ O ₅	up	ko00121
52	Propiolic acid	C ₃ H ₂ O ₂	up	ko00410, ko00640, ko01100
53	Gamma-Glu-Leu	C ₁₁ H ₂₀ N ₂ O ₅	up	--
54	1-Oleoyl Lysophosphatidic Acid (sodium salt)	C ₂₁ H ₄₁ O ₇ P	up	--
55	Magnoshinin	C ₂₄ H ₃₀ O ₆	up	--
56	Glycoursodeoxycholic acid	C ₂₆ H ₄₃ NO ₅	up	--
57	Avermectin B1b aglycone	C ₃₃ H ₄₆ O ₈	up	ko00522, ko01100, ko01110
58	PE-NMe(11D3/11M5)	C ₄₇ H ₈₂ NO ₁₀ P	up	--
59	Arg Leu Lys Trp	C ₂₉ H ₄₇ N ₉ O ₅	up	--
60	alpha, beta-Dihydroxyethyl-TPP;alpha,beta-Dihydroxyethyl-ThDP;2-(1,2-Dihydroxyethyl)-TPP	C ₁₄ H ₂₃ N ₄ O ₉ P ₂ S	up	--

Table S1 (contd.)

NO.	Metabolite	Formula	Trend	KEGG map
61	PE-NMe (18:0/22:5(4Z,7Z,10Z,13Z,16Z))	C ₄₆ H ₈₂ NO ₈ P	up	--
62	D-Glyceraldehyde 3-phosphate	C ₃ H ₇ O ₆ P	up	ko00010, ko00030, ko00051, ko00052, ko00331, ko00562, ko00680, ko00710, ko00730, ko00750, ko00900, ko01060, ko01061, ko01062, ko01063, ko01064, ko01065, ko01066, ko01070, ko01100, ko01110, ko01120, ko01200, ko01230
63	Asp Asn Tyr Lys	C ₂₃ H ₃₄ N ₆ O ₉	up	--
64	2-hydroxyhexadecanoic acid	C ₁₆ H ₃₂ O ₃	up	--
65	Ergosta-5,7,22,24(28)-tetraen-3beta-ol; Ergosta-5,7,22,24(24(1))-tetraen-3beta-ol;5,7,22,24(28)-Ergostatetraenol	C ₂₈ H ₄₂ O	up	ko00100, ko01100, ko01110
66	Jervine	C ₂₇ H ₃₉ NO ₃	up	ko01066
67	Phosphoglycolic acid	C ₂ H ₅ O ₆ P	up	ko00630, ko01100, ko01110, ko01200
68	PE-NMe (14:0/14:1(9Z))	C ₃₄ H ₆₆ NO ₈ P	up	--
69	Ursodeoxycholic acid	C ₂₄ H ₄₀ O ₄	up	ko00121
70	20-O-Methyl-19-chloroproansamitocin	C ₂₆ H ₃₄ ClNO ₆	up	ko01051, ko01110
71	3-Oxocholic acid	C ₂₄ H ₃₈ O ₅	up	--
72	Glycodeoxycholic acid	C ₂₆ H ₄₃ NO ₅	up	--
73	Dimethylarsinate	C ₂ H ₇ AsO ₂	up	--
74	Pyrazole	C ₃ H ₄ N ₂	up	--
75	Osthenol-7-O-beta-D-gentiobioside	C ₂₆ H ₃₄ O ₁₃	up	--
76	Acetyl-maltose;6-O-Acetyl-alpha-D-glucopyranosyl-(1->4)-D-glucose	C ₁₄ H ₂₄ O ₁₂	up	--

Table S1 (contd.)

NO.	Metabolite	Formula	Trend	KEGG map
77	Ala Pro Arg	C ₁₄ H ₂₆ N ₆ O ₄	up	--
78	Ala Gln Asp Thr Gln	C ₂₁ H ₃₅ N ₇ O ₁₁	up	--
79	1,1,1-Trichloroethane	C ₂ H ₃ Cl ₃	up	ko00625, ko01120
80	Naringenin-7-O- -D-Glucuronide	C ₂₁ H ₂₀ O ₁₁	up	--
81	CL(i-14:0/i-17:0/i-14:0/a-13:0) [rac]	C ₆₇ H ₁₃₀ O ₁₇ P ₂	up	--
82	Phe Cys Leu Phe Arg	C ₃₃ H ₄₈ N ₈ O ₆ S	up	--
83	(+)-Neomenthyl O-beta-D-glucoside	C ₁₆ H ₃₀ O ₆	up	--
84	Methyl diacetox-10-gingerdiol	C ₂₆ H ₄₂ O ₆	up	--
85	ponasterone A	C ₂₇ H ₄₄ O ₆	up	--
86	Manidipine (Manyper)	C ₃₅ H ₃₈ N ₄ O ₆	up	--
87	Pro Pro Asp Gln Gln	C ₂₄ H ₃₇ N ₇ O ₁₀	down	--
88	PC (18:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	C ₄₈ H ₈₄ NO ₈ P	down	--
89	1-Stearoyl-2-Arachidonoyl PC	C ₄₆ H ₈₄ NO ₈ P	down	--
90	1-(1Z-Octadecenyl)-2-(5Z,8Z,11Z,14Z-eicosatetraenyl)-sn-glycero-3-phosphocholine	C ₄₆ H ₈₄ NO ₇ P	down	--
91	Strictosamide	C ₂₆ H ₃₀ N ₂ O ₈	down	ko01060, ko01063
92	1-Palmitoyl-2-docosaheptaenoyl-sn-glycero-3-phosphocholine	C ₄₆ H ₈₀ NO ₈ P	down	--
93	Cidofovir	C ₈ H ₁₄ N ₃ O ₆ P	down	--
94	2-Oleoyl-1-palmitoyl-sn-glycero-3-phosphocholine	C ₄₂ H ₈₂ NO ₈ P	down	--
95	His Ser Asn	C ₁₃ H ₂₀ N ₆ O ₆	down	--
96	1-Palmitoyl-2-linoleoyl-sn-glycero-3-phosphocholine	C ₄₂ H ₈₀ NO ₈ P	down	--
97	1-Oleoyl-2-palmitoyl-sn-glycero-3-phosphocholine	C ₄₂ H ₈₂ NO ₈ P	down	--

Table S1 (*contd.*)

NO.	Metabolite	Formula	Trend	KEGG map
98	L-Tryptophan	C ₁₁ H ₁₂ N ₂ O ₂	down	ko00260, ko00380, ko00400, ko00404, ko00901, ko00966, ko00970, ko00998, ko01060, ko01061, ko01063, ko01070, ko01100, ko01110, ko01210, ko01230, ko04361, ko04726, ko04974, ko04978, ko05143, ko05230
99	1,2-Dilinoleoyl-sn-glycero-3-phosphocholine	C ₄₄ H ₈₀ NO ₈ P	down	--
100	Ile Leu Asn Asp	C ₂₀ H ₃₅ N ₅ O ₈	down	--
101	N-Acetyl-L-methionine	C ₇ H ₁₃ NO ₃ S	down	--
102	LH 21	C ₂₀ H ₂₀ C ₁₃ N ₃	down	--

Note : -- : the metabolite was not mapped to the corresponding pathway map in KEGG.