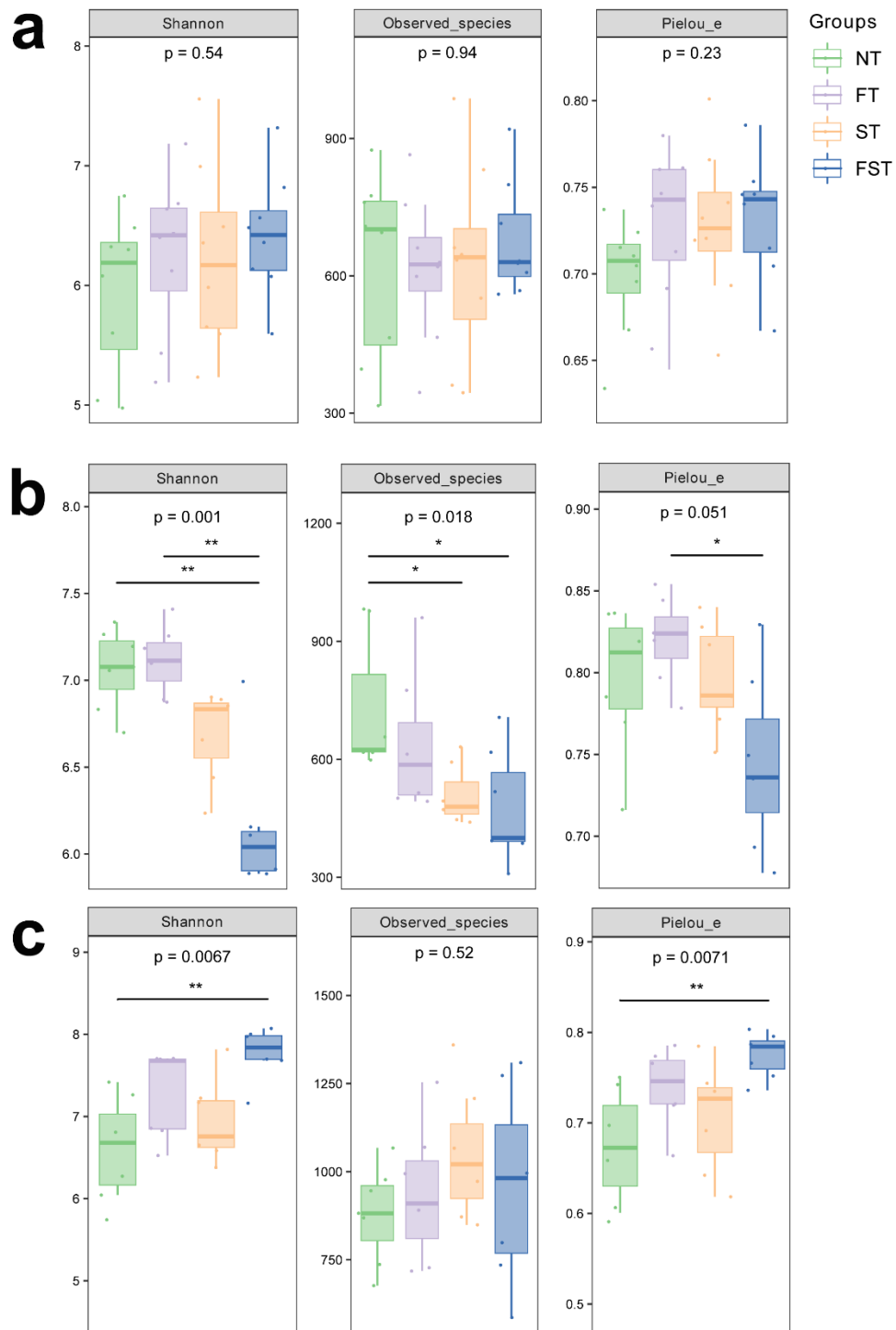
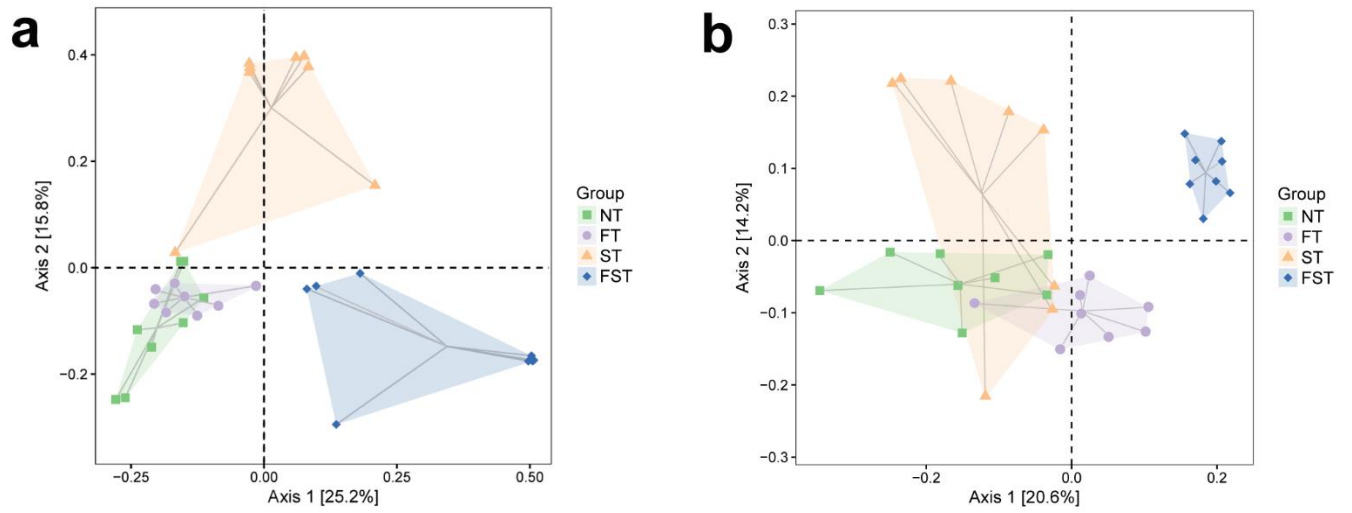


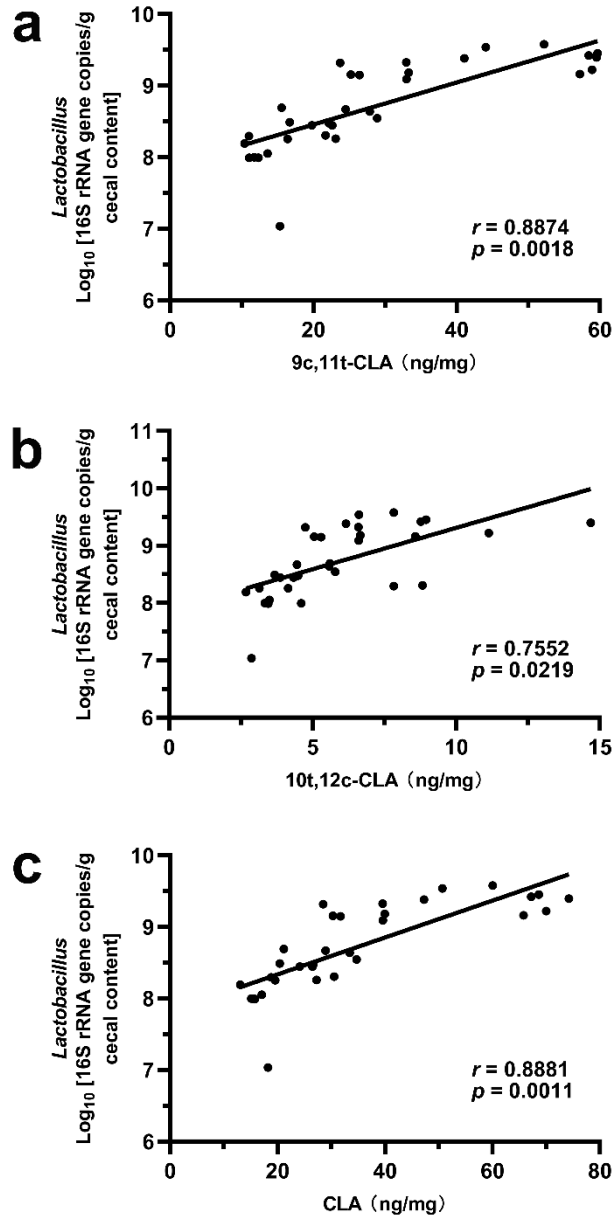
**FIG S1** Effect of florfenicol on intestinal permeability and expression of cytokines in ileum of *S. Enteritidis*-infected chickens. Serum D-lactate (a), serum DAO (b), serum LPS (c), IL-1β (d), serum IL-6 (e), IL-8 (f), IL-10 (g), TNF-α (h) and INF-γ (i) were compared at 3 dpi. Data are expressed as means ± standard deviation. Statistical significance was assessed by ANOVA and denoted as: \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001.



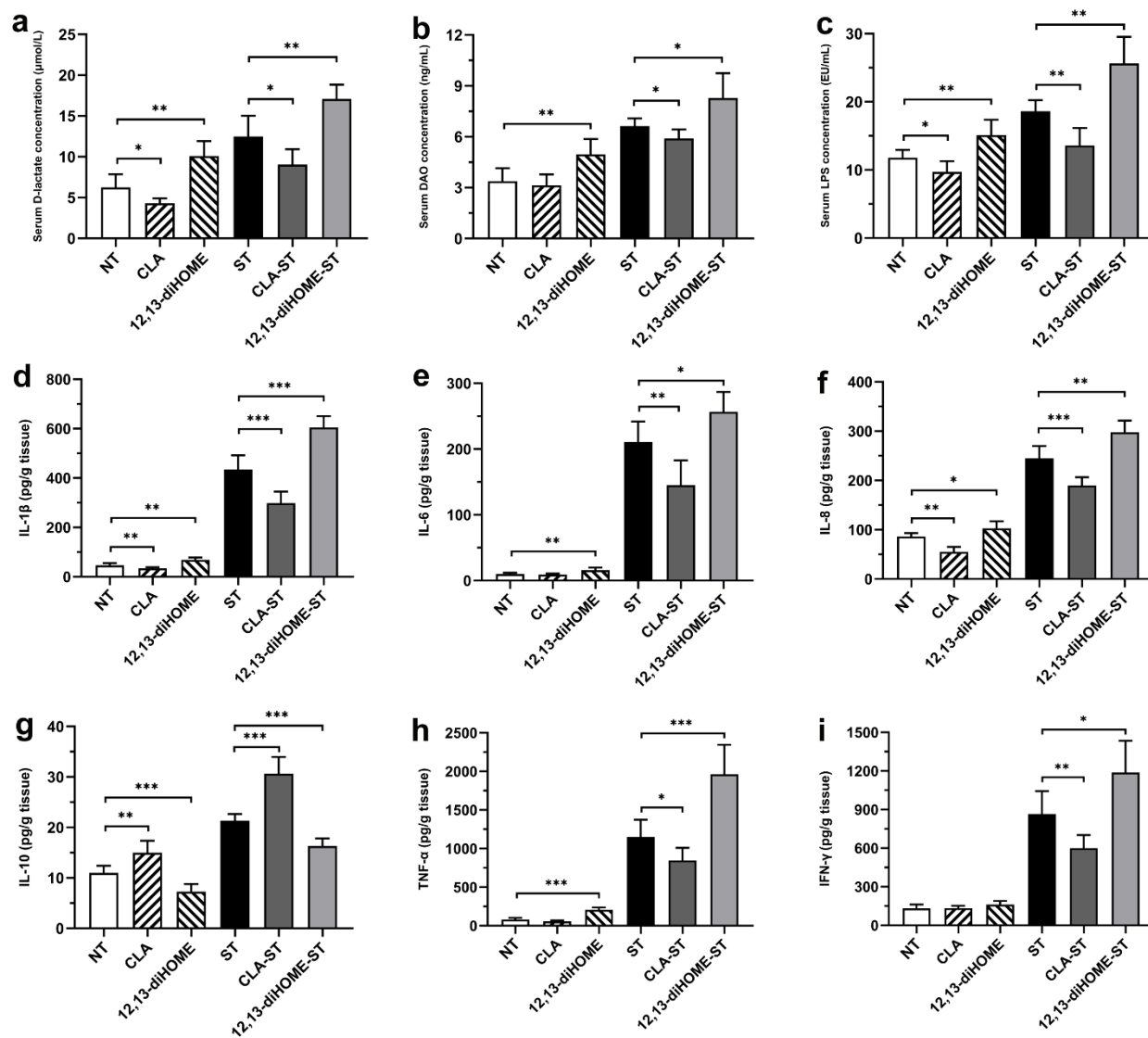
**FIG S2** Effect of florfenicol on  $\alpha$ -diversity of cecal microbiota in normal and *S. Enteritidis*-infected chicks. Boxplots of Shannon index, Observed species, and Pielou index of cecal microbiota in different groups from 3 dpi (a), 10 dpi (b) and 17 dpi (c). \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ ; Kruskal-Wallis test.



**FIG S3** Effect of florfenicol on the  $\beta$ -diversity of cecal microbial communities in response to *S. Enteritidis* infection. PCoA for comparison of the changes in bacterial communities in different groups at 10 dpi (a) and 17 dpi (b) was generated using the Bray-Curtis distance method.

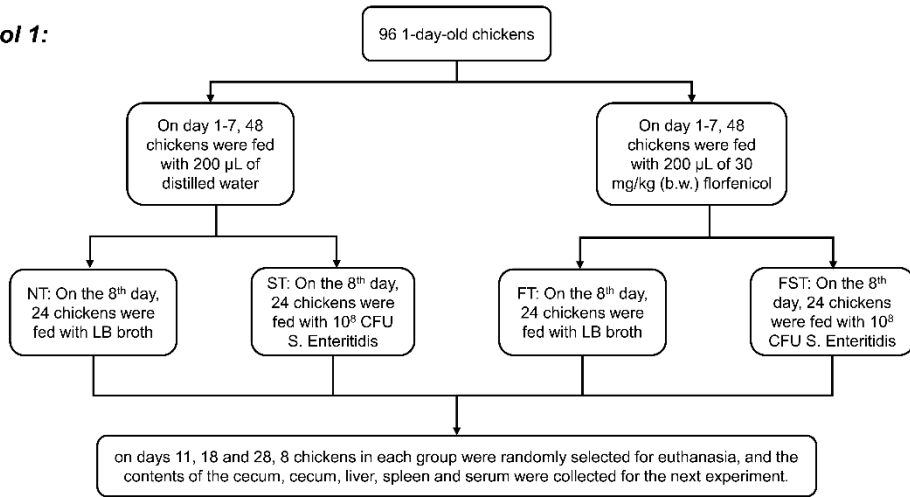


**FIG S4** *Lactobacillus* positively correlates with CLA. Correlations between abundance of *Lactobacillus* present in the cecal content of chicks and: (a) 9c, 11t-CLA (ng/mg); (b) 10t, 12c-CLA (ng/mg); (c) total CLA (ng/mg).

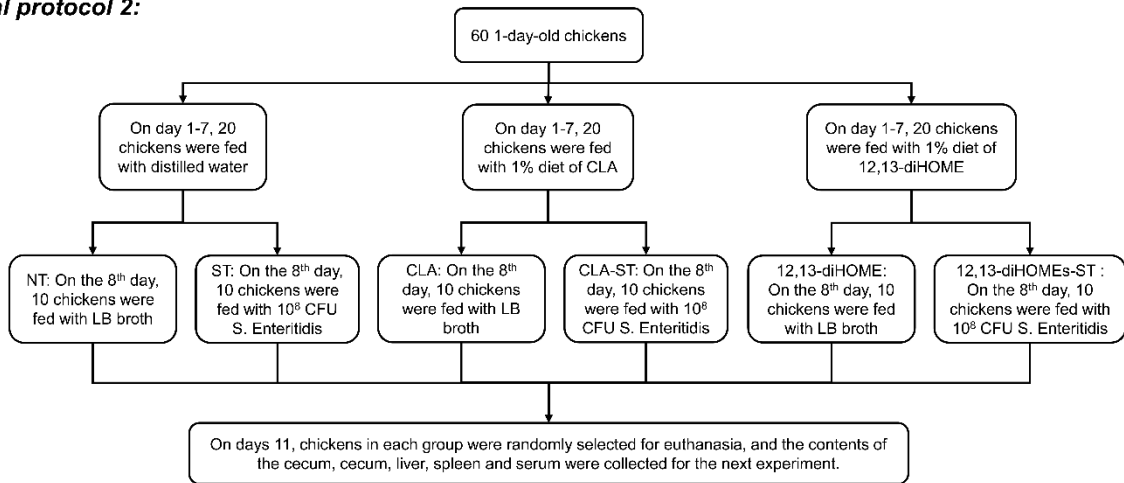


**FIG S5** Effect of CLA and 12,13-diHOME on intestinal permeability and expression of cytokines in ileum of *S. Enteritidis*-infected chickens. Serum D-lactate (a), serum DAO (b), serum LPS (c), IL-1β (d), serum IL-6 (e), IL-8 (f), IL-10 (g), TNF-α (h) and INF-γ (i) were compared at 3 dpi. Data are expressed as means ± standard deviation. Statistical significance was assessed by ANOVA and denoted as: \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001.

**Animal protocol 1:**



**Animal protocol 2:**



**FIG S6** Animal experiment design and layout. *Animal protocol 1*: effect of florfenicol exposure on *Salmonella* infection; *Animal protocol 2*: effect of CLA and 12,13-diHOME on *Salmonella* infection.

**Table S1** Primers used for bacterial and host qPCR

<b>Bacterial 16S or 23S rRNA target</b>	<b>Primer</b>	<b>Sequence (5'-3')</b>
<i>Eubacteria</i> (total bacteria)	Forward	ACTCCTACGGGAGGCAGCAGT
	Reverse	ATTACCGCGGCTGCTGGC
<i>Enterobacteriaceae</i>	Forward	TGCCGTAACCTTCGGGAGAAGGCA
	Reverse	TCAAGGCTCAATGTTTCAGTGTC
<i>Lactobacillus</i>	Forward	AGCAGTAGGGAATCTTCCA
	Reverse	CACCGCTACACATGGAG
<i>Dorea</i>	Forward	GCAGCTAACGCAATAAGCAG
	Reverse	CTTCCATTACGAAGCGGTC
<i>Clostridium butyricum</i>	Forward	GTGCCGCCGCTAACGCATTAAGTAT
	Reverse	ACCATGCACCACCTGTCTTCCTGCC
<i>Bacteroidetes</i>	Forward	GGARCATGTGGTTTAATTCGATGAT
	Reverse	AGCTGACGACAACCATGCAG
<b>Host gene target</b>	<b>Primer</b>	<b>Sequence (5'-3')</b>
ZO-1	Forward	GCCTGAATCAAACCCAGCAA
	Reverse	TATGCGCGGTAAGGATGAT
Occludin	Forward	GATGGACAGCATCAACGACC
	Reverse	CATGCGCTTGATGTGGAAGA
Claudin 3	Forward	GAAGGGCTGTGGATGAACTG
	Reverse	GAGACGATGGTGATCTTGGC
MUC2	Forward	AATGCTGAGTTCTTGCCTAA
	Reverse	GTTGCAGTTCATATCCTGGT
TFF2	Forward	CCCTGCTGATCCTCGTAT
	Reverse	GCTGTTATTTCCCAGTTGA
IL-22	Forward	CAGGAATCGCACCTACACCT
	Reverse	TCATGTAGCAGCGGTTGTTC
IL-17A	Forward	CCATTCCAGGTGCGTGAACCT
	Reverse	TTTCTTCTCCAGGCGGTACG
IFN- $\alpha$	Forward	CCAGCACCTCGAGCAAT
	Reverse	GCGCTGTAATCGTTGTCT
GAPDH	Forward	TCTCTGGCAAAGTCCAAGTG
	Reverse	CTTGAAGTGTCCGTGTGTAGAA

**Table S2** Differential metabolites of cecal content in different group sets

<b>Compound</b>	<b>VIP value</b>	<b>Fold change (FT-NT)</b>
LysoPE(0:0/16:0)	1.39611	1.829127912
Phytosphingosine	1.82172	2.391519065
Kynurenic acid	1.58781	1.32017953
Stearidonic acid	1.45078	0.762002229
Octadecanamide	1.50001	1.048119468
Stearoylcarnitine	1.69755	2.230264288
L-Glutamate	1.69534	2.647962778
Tetracosahexaenoic acid	1.37745	-4.256204048
3-Indolepropionic acid	1.48629	1.654602046
Syringic acid	1.9675	2.591620047
Methamphetamine	1.38677	-4.294895853
L-Palmitoylcarnitine	1.3594	2.433415468
Dodecanedioic acid	1.81947	-2.553967404
Anandamide	1.72204	-4.126681323
hydrocinnamic acid	1.56801	0.956241528
Linoleic acid	1.55562	3.036584872
Ricinoleic acid	1.4407	2.541515312
p-Aminobenzoic acid	1.59528	1.416099173
13-HDoHE	1.5072	1.614593796
N-Acetyl-L-methionine	1.51667	0.77972235
Androstenol	1.48051	1.805266093
L-Isoleucine	1.59496	1.432195562
Cinnamic acid	1.50697	1.472848477
Creatine	1.49684	1.06131712
Pantothenic Acid	1.67721	2.57961707
L-Tryptophan	1.63324	1.449201617
12,13-EpOME	1.62341	4.469650467
L-Tyrosine	1.40308	0.699634193
Adenosine	1.47445	2.243025557
N6,N6,N6-Trimethyl-L-lysine	1.42211	-1.689249154
3-Hydroxyanthranilic acid	1.69687	1.719421014
Glycylleucine	1.55493	1.659377013
12,13-diHOME	1.56895	7.994652917
LysoPE(20:0/0:0)	1.89989	1.809808066
Xanthurenic acid	2.0962	1.717569376
Acetylcarnitine	1.62655	0.827224224
LysoPC(14:0)	1.59089	1.293272182
1-Methylguanine	1.37433	-1.271014565
Vitamin A	1.53692	1.126347198
Hexanoylcarnitine	1.51544	1.381526102



Acetylcholine	1.53842	1.440701802
L-Phenylalanine	1.50505	1.470457546
Adenine	1.45115	2.837115373
LysoPE(18:0/0:0)	1.80815	1.431342848
QH(2)	1.4405	2.052805741
N-Acetyl-D-glucosamine	1.36669	-0.575336932
L-Dopa	1.60085	1.13622862
L-Arginine	1.47707	1.135803137
MG(P-18:0e/0:0/0:0)	1.48374	2.372686188
L-Valine	1.36891	1.218955241
Pyroglutamic acid	1.36302	0.443618789
5-Aminopentanoic acid	1.61074	0.984877935
acetophenone	1.50397	2.077766733
gamma-Aminobutyric acid	1.65933	1.315620616
DHAP(10:0)	1.38044	0.783071918
Benzoic acid	1.83512	1.264673024
Niacinamide	1.46789	0.904334539
Choline	1.40391	1.271636765
gamma-Glutamylcysteine	1.96829	0.689634575
Xanthosine	1.59451	-1.121281824
Taurocholic acid	1.58083	2.700112967
Tetradecanedioic acid	1.87358	-4.548811504
Tauroursodeoxycholic acid	1.97904	2.998046677
Sebacic acid	2.33912	-1.991768331
Ribonic acid	1.66162	3.146818765
L-Ascorbic acid	1.78324	-1.881321665
Oxoadipic acid	1.65964	1.179545557
DL-2-Aminoadipic acid	1.80898	1.146523006
Pimelic acid	1.46471	-0.637229481
3-Hydroxypicolinic acid	2.0197	-0.790658614
L-Arabitol	1.45687	2.266739636

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<b>Compound</b>	<b>VIP value</b>	<b>Fold change (ST-NT)</b>
LysoPE(0:0/16:0)	1.4496	3.481737371
Phytosphingosine	1.52776	1.592384062
Alpha-Tocotrienol	1.7476	-1.785491958
Palmitic amide	1.43074	0.778172326
Glucose 6-phosphate	1.43218	2.277174679
Octadecanamide	1.70732	0.982474063
MG(0:0/14:0/0:0)	1.80987	2.680202659
Methamphetamine	1.37498	-6.311569107
Anandamide	1.65535	-3.882060603
3-Oxohexadecanoic acid	1.57015	3.850803532

Prostaglandin F1a	1.52815	2.46413986
p-Aminobenzoic acid	1.48707	1.954157026
13-HDoHE	1.40768	1.918124518
N-Acetyl-L-methionine	1.40131	0.754827151
Phosphocholine	1.55202	3.438641792
Androstenol	1.42131	2.13902204
Pantothenic Acid	1.50101	2.195213934
L-Glutamate	1.38699	2.211475066
3-Hydroxypicolinic acid	2.06276	-1.813504968
Xanthurenic acid	1.66744	1.370329373
Acetylcarnitine	1.6146	1.756399319
Hexanoylcarnitine	1.55398	2.618099366
Agmatine	1.41379	-1.548909222
Acetylcholine	1.52897	1.533418091
L-Arginine	1.58816	1.295701572
Jasmonic acid	1.60925	-1.580062717
Gamma-Tocotrienol	2.00752	-2.31237927
3-Indoleacetic Acid	1.52672	-1.589484144
N-Acetylputrescine	1.40706	-0.906352868
L-Proline	1.92109	-1.228515711
Maltitol	1.52127	-1.895084115
Deoxycholic acid	1.419	-4.040597938
Vitamin A	1.52456	-0.867762178
Prostaglandin A2	1.88831	-1.150186154
Riboflavin	1.72363	-1.802289433
Lithocholic acid	1.44492	-5.87927103
Abscisic acid	1.78497	-0.756908613
Sebacic acid	2.16878	-1.598290569
Oxoadipic acid	1.60838	1.24635069
DL-2-Amino adipic acid	1.59324	1.030199257
Mevalonic acid	1.48103	1.563893484
L-Arabitol	1.72051	4.158005369

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<b>Compound</b>	<b>VIP value</b>	<b>Fold change (FST-NT)</b>
Cinnamic acid	1.43992	2.703635592
LysoPE(0:0/16:0)	1.43182	2.5117326
Phytosphingosine	2.04975	1.986185762
Leucylproline	1.98478	1.851524634
Kynurenic acid	1.7098	1.219018183
DL-2-Amino octanoic acid	1.38835	0.768609868
3-Indolepropionic acid	1.90076	4.461901507
Syringic acid	2.23866	3.078865508
Methamphetamine	1.39256	-4.55929079

L-Palmitoylcarnitine	1.47038	2.629265249
Alanylproline	1.5974	0.510109715
Anandamide	1.72808	-4.291065328
Linoleic acid	1.45238	1.478622708
p-Aminobenzoic acid	1.72266	0.85562942
N-Acetyl-L-methionine	1.74627	0.879515457
Dodecanoylcarnitine	1.57485	-4.497912518
L-Isoleucine	1.67578	2.211052657
L-Phenylalanine	1.43065	2.686265148
Pantothenic Acid	2.0976	2.30738253
L-Norleucine	1.40984	1.155267625
L-Tryptophan	1.60781	2.297523805
12,13-EpOME	1.60988	2.448364017
L-Methionine	1.5779	1.819252502
Urocanic acid	1.76454	0.942676897
L-Tyrosine	1.78508	1.557881882
Glycylleucine	1.43032	3.581452911
N6,N6,N6-Trimethyl-L-lysine	1.67502	-3.210622506
12,13-diHOME	1.53023	5.649873041
Bilirubin	1.3852	-1.064770931
5'-Methylthioadenosine	1.55559	0.495600108
Glutamylleucine	1.39844	2.673354257
LysoPE(20:0/0:0)	1.39773	2.946797528
Norepinephrine	1.39502	0.444847909
Acetylcarnitine	1.46912	0.638635163
4-Pyridoxic acid	1.51644	-0.716787952
LysoPE(18:0/0:0)	1.46056	2.545971698
N-Acetyl-D-glucosamine	1.42657	-0.699549345
L-Valine	1.51147	0.800046414
Thymine	1.70023	1.063475055
Pyroglutamic acid	1.62851	0.578966596
Uracil	1.52934	0.276832643
Anthranilic acid	1.87681	1.472959506
Acetoacetic acid	1.36386	-0.96299723
L-Proline	1.90616	0.655623559
gamma-Aminobutyric acid	1.40762	0.550493831
Benzoic acid	1.92242	1.971645349
Choline	1.61916	2.227098982
Cholic acid	1.59267	1.721624591
9,12,13-TriHOME	1.76847	0.909013359
7-Ketodeoxycholic acid	1.47884	3.057090822
Prostaglandin A2	1.46131	-0.729895116
gamma-Glutamylcysteine	1.47696	0.44016878
Taurocholic acid	1.46752	2.695106091

MG(0:0/15:0/0:0)	1.6415	1.404584772
Abscisic acid	1.46093	-1.571901825
Tauroursodeoxycholic acid	1.85322	2.470980718
N-Acetyl-L-phenylalanine	1.47184	1.114728441
Xanthurenic acid	1.55581	0.773738658
Caffeic Acid	1.45106	1.156454677
Citric acid	1.59456	1.478525358
Ribonic acid	1.4903	1.641496722
L-Ascorbic acid	1.99091	-3.321106442
L-3-Phenyllactic acid	1.5724	1.60013447
Oxoadipic acid	1.48361	1.14726273
Oxoglutaric acid	1.54047	1.68390509
DL-2-Aminoadipic acid	2.13987	1.19424498
Pimelic acid	2.09643	-1.028867534
D-2-Hydroxyglutaric acid	2.27341	1.300347595
Fumaric acid	1.59133	-0.856132678

<b>Compound</b>	<b>VIP value</b>	<b>Fold change (FST-ST)</b>
9-HOTE	1.48485	0.303790663
Leucylproline	1.70616	1.144383582
Glucose 6-phosphate	1.51163	-2.326664278
Octadecanamide	1.87365	-0.507471409
DL-2-Aminooctanoic acid	1.73001	1.145522942
Inosine	1.60348	0.488953943
3-Indolepropionic acid	1.98678	4.448026386
Abscisic acid	1.94412	0.693852937
MG(0:0/14:0/0:0)	1.88269	-2.396425517
Sphinganine	1.46259	-1.353688662
Alpha-Tocotrienol	1.78427	1.573340492
MG(0:0/16:0/0:0)	1.75446	-1.173105075
Docosanamide	1.94906	-1.623745682
3-Oxohexadecanoic acid	1.67798	-4.140822579
Phosphocholine	1.53266	-2.469506451
Dodecanoylcarnitine	1.77728	-3.172944392
Creatine	1.51359	-0.640881169
12,13-EpOME	1.61941	3.823295465
12,13-diHOME	1.54795	6.178657304
Cholestenone	1.65806	1.411480517
Stigmasterol	1.76371	0.812126162
Alanylproline	1.59357	0.510184612
3-Hydroxypicolinic acid	1.5083	1.31676859
Acetylcarnitine	1.494	-1.117764156
Agmatine	1.59512	1.906900037

Acetylcholine	1.65862	-1.674756867
Leukotriene A4	1.82758	0.875895561
Jasmonic acid	1.60353	3.291211347
Gamma-Tocotrienol	1.54301	3.294728599
3-Indoleacetic Acid	2.20801	1.887321531
Tyramine	1.52292	1.129114722
Thymine	1.86664	1.449681321
Indole	1.78473	0.41691403
Anthranilic acid	2.05673	1.873975616
L-Proline	1.60613	0.463939663
Maltitol	2.20513	2.16449355
alpha-Tocopherol	1.70547	-1.373407256
Octadecanedioic acid	1.46753	0.764335022
Deoxycholic acid	1.85869	4.260337761
Urobilin	1.68187	1.792473085
gamma-Glutamylcysteine	2.00579	0.554982865
Nutriacholic acid	1.49181	1.67148456
Prostaglandin G2	1.48664	0.700765456
Prostaglandin E1	1.63335	0.890821767
Abscisic acid	1.89171	0.999427992
12-Hydroxystearic acid	1.72965	-1.090242628
Jasmonic acid	1.67078	2.943268971
Sebacic acid	1.49948	1.093535982
Decenedioic acid	1.55915	1.196605122
Xanthurenic acid	1.65874	-0.791642226
Kynurenic acid	1.58615	0.906834108
D-Mannitol	1.54799	-1.883904931
Caffeic Acid	1.85991	1.956615942
L-Ascorbic acid	1.51678	-4.243989453
3-Hydroxypicolinic acid	2.06757	2.366329392
L-Arabitol	1.75568	-4.03475644
Fumaric acid	1.47533	-1.038164572

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