Supporting information

Figure S1 Effects of APH, APH-CA and CA on brain neurotransmitters of scopolamine induced amnesia mice without changes.

Figure S2 The correlation analysis between gut microbiota and fecal metabolites on Species level. The right side of the figure is the metabolite name, and the bottom is the gut microbiota. Each grid in the figure represents the correlation between two attributes (metabolites and gut microbiota), and different colors represent the correlation coefficient between attributes.

Figure S3 The correlation analysis between gut microbiota and brain neurotransmitters on Genus level. The x-axis and y-axis are neurotransmitters and microbiota on Genus level, respectively. The correlation R value and P value are obtained through calculation. The R value is shown in different colors in the figure. If the p value is less than 0.05, it is marked with * and the legend on the right is the color range of different R values.

Figure S4 The correlation analysis between fecal metabolites and brain neurotransmitters.

Figure S5 The distribution proportion of dominant species in each sample and the distribution proportion of each dominant species in different groups.

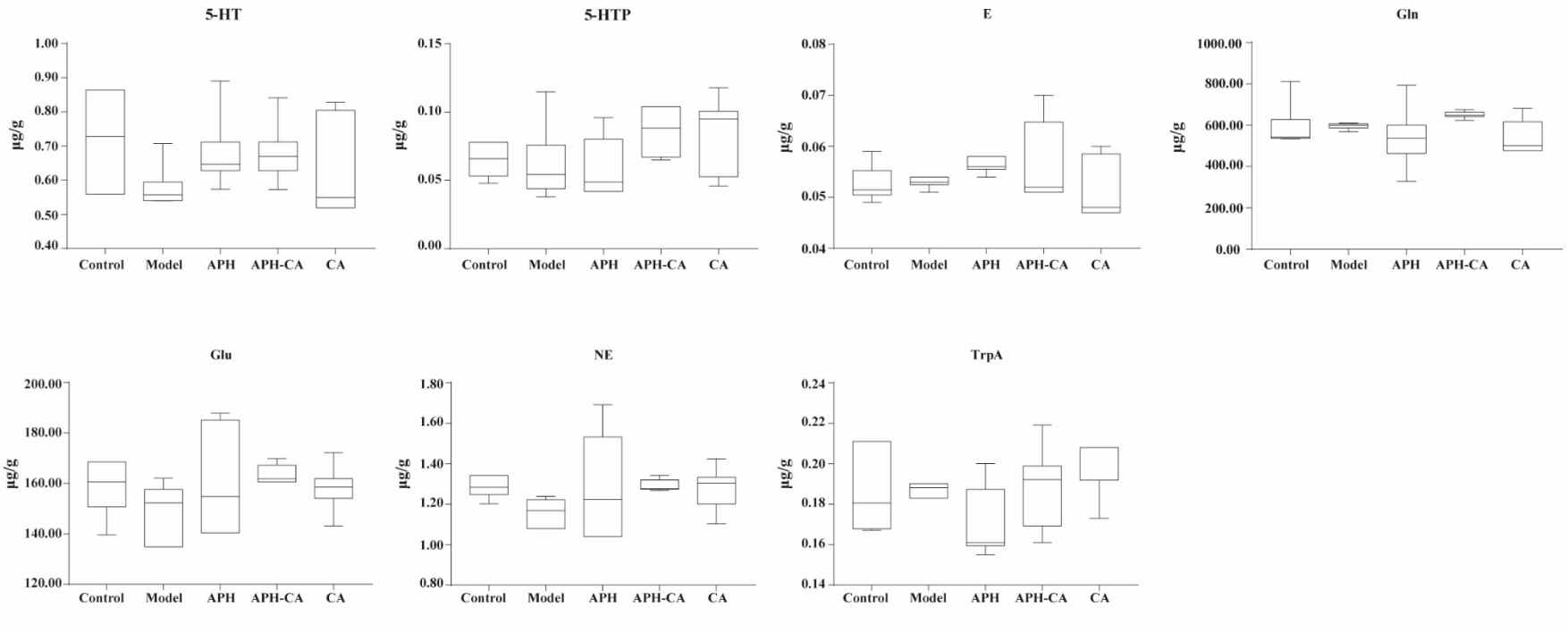
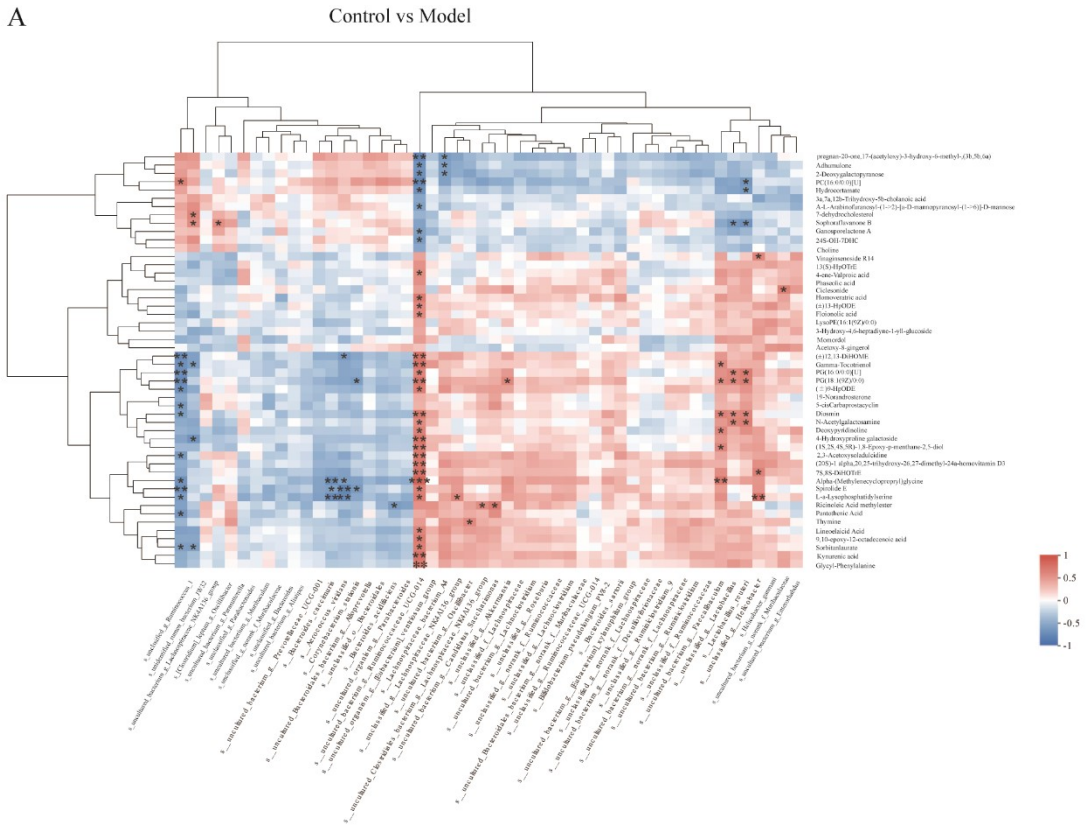

5-HT
μg/g
1.00
0.90
0.80
0.70
0.60
0.50
0.40
Control
Model
APH
APH-CA
CA
5-HTP
μg/g
0.15
0.10
0.05
0.00
Control
Model
APH
APH-CA
CA
E
μg/g
0.08
0.07
0.06
0.05
0.04
Control
Model
APH
APH-CA
CA
Gln
μg/g
1000.00
800.00
600.00
400.00
200.00
0.00
Control
Model
APH
APH-CA
CA
Glu
μg/g
200.00
180.00
160.00
140.00
120.00
Control
Model
APH
APH-CA
CA
NE
μg/g
1.80
1.60
1.40
1.20
1.00
0.80
Control
Model
APH
APH-CA
CA
TrpA
μg/g
0.24
0.22
0.20
0.18
0.16
0.14
Control
Model
APH
APH-CA
CA

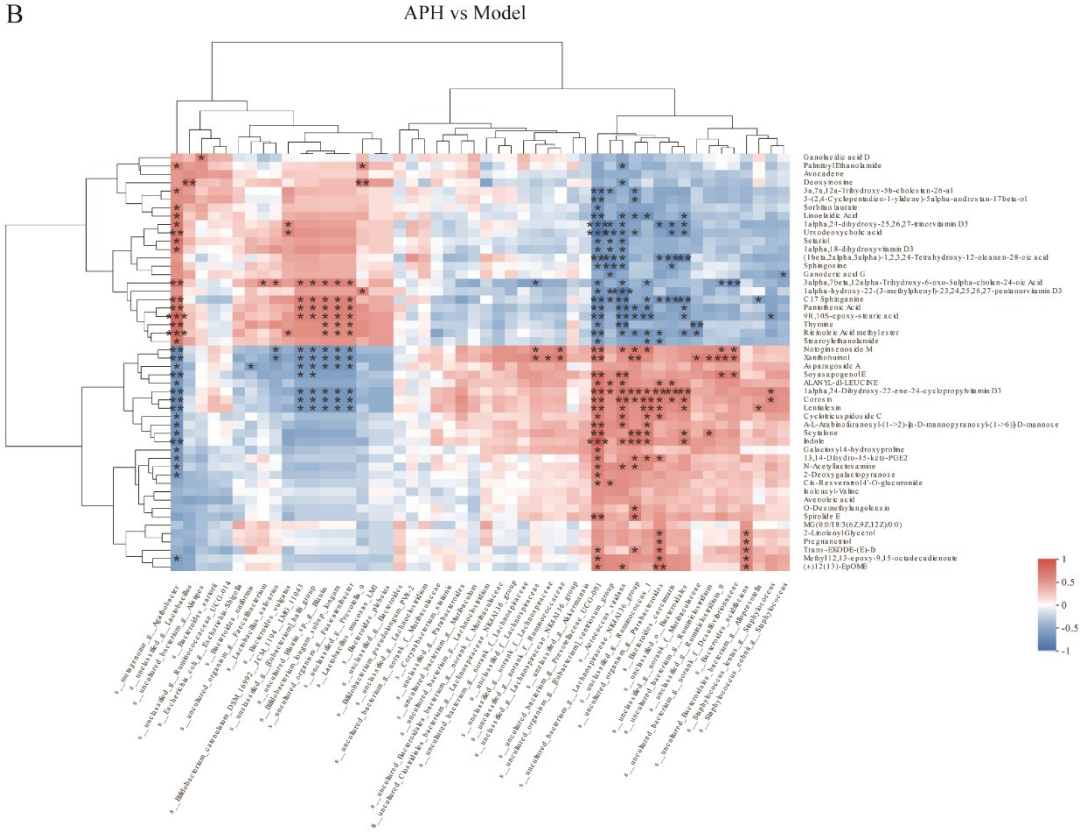
Figure S1



23

24 **Figure** S2 A

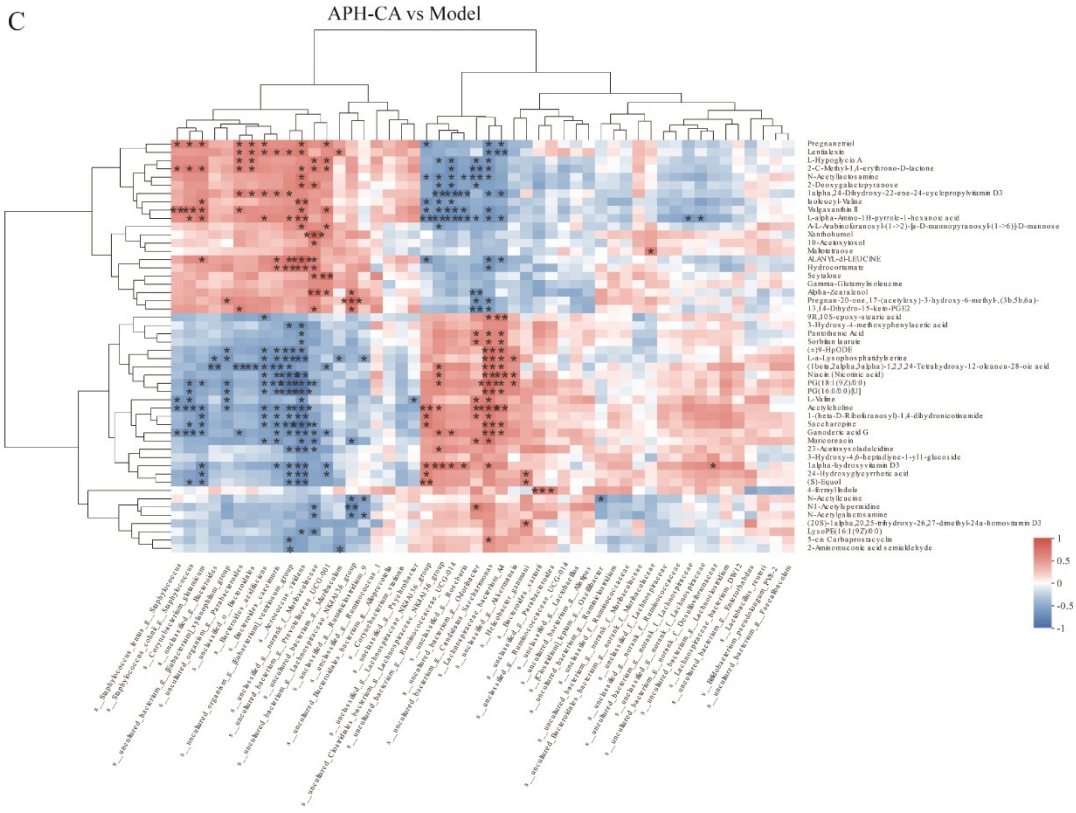
B



25

26 **Figure** S2 B

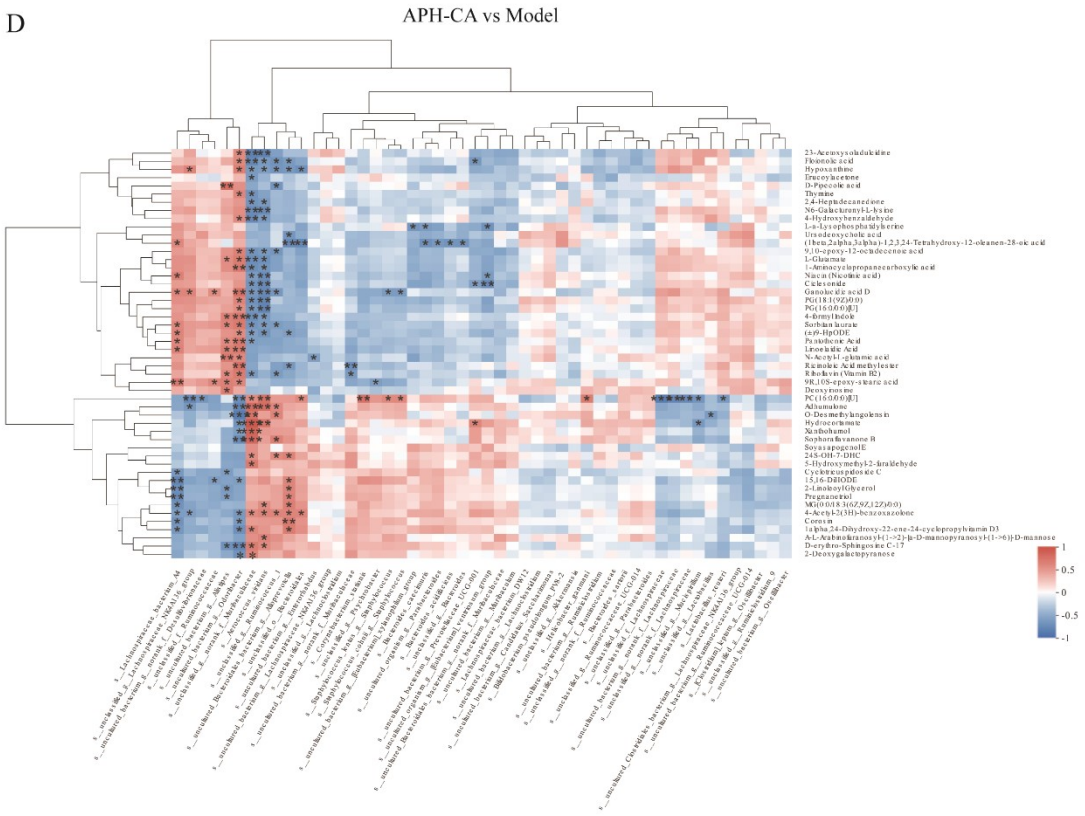
C



27

28 **Figure** S2 C

D



29

30

31 **Figure** S2 D

32

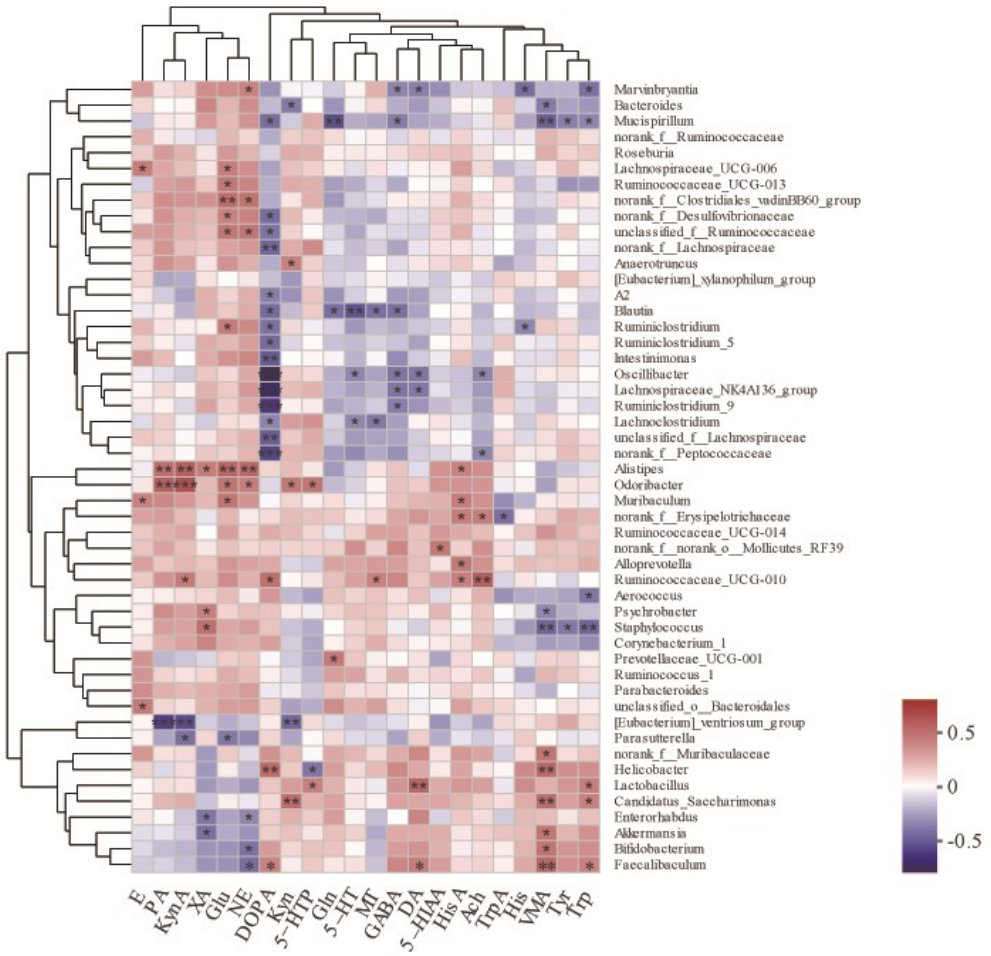

Marvinbryantia
Bacteroides
Mucispirillum
norank_f__Ruminococcaceae
Roseburia
Lachnospiraceae_UCG-006
Ruminococcaceae_UCG-013
norank_f__Clostridiales_vadinBB60_group
norank_f__Desulfovibrionaceae
unclassified_f__Ruminococcaceae
norank_f__Lachnospiraceae
Anaerotruncus
[Eubacterium]_xylanophilum_group
A2
Blautia
Ruminiclostridium
Ruminiclostridium_5
Intestinimonas
Oscillibacter
Lachnospiraceae_NK4A136_group
Ruminiclostridium_9
Lachnoclostridium
unclassified_f__Lachnospiraceae
norank_f__Peptococcaceae
Alistipes
Odoribacter
Muribaculum
norank_f__Erysipelotrichaceae
Ruminococcaceae_UCG-014
norank_f__norank_o__Mollicutes_RF39
Alloprevotella
Ruminococcaceae_UCG-010
Aerococcus
Psychrobacter
Staphylococcus
Corynebacterium_1
Prevotellaceae_UCG-001
Ruminococcus_1
Parabacteroides
unclassified_o__Bacteroidales
[Eubacterium]_ventriosum_group
Parasutterella
norank_f__Muribaculaceae
Helicobacter
Lactobacillus
Candidatus_Saccharimonas
Enterorhabdus
Akkermansia
Bifidobacterium
Faecalibaculum
E
PA
KynA
XA
Glu
NE
DOPA
Kyn
5−HTP
Gln
5−HT
MT
GABA
DA
5−HIAA
His A
Ach
TrpA
His
VMA
Tyr
Trp
0.5
0
-0.5

Figure S3

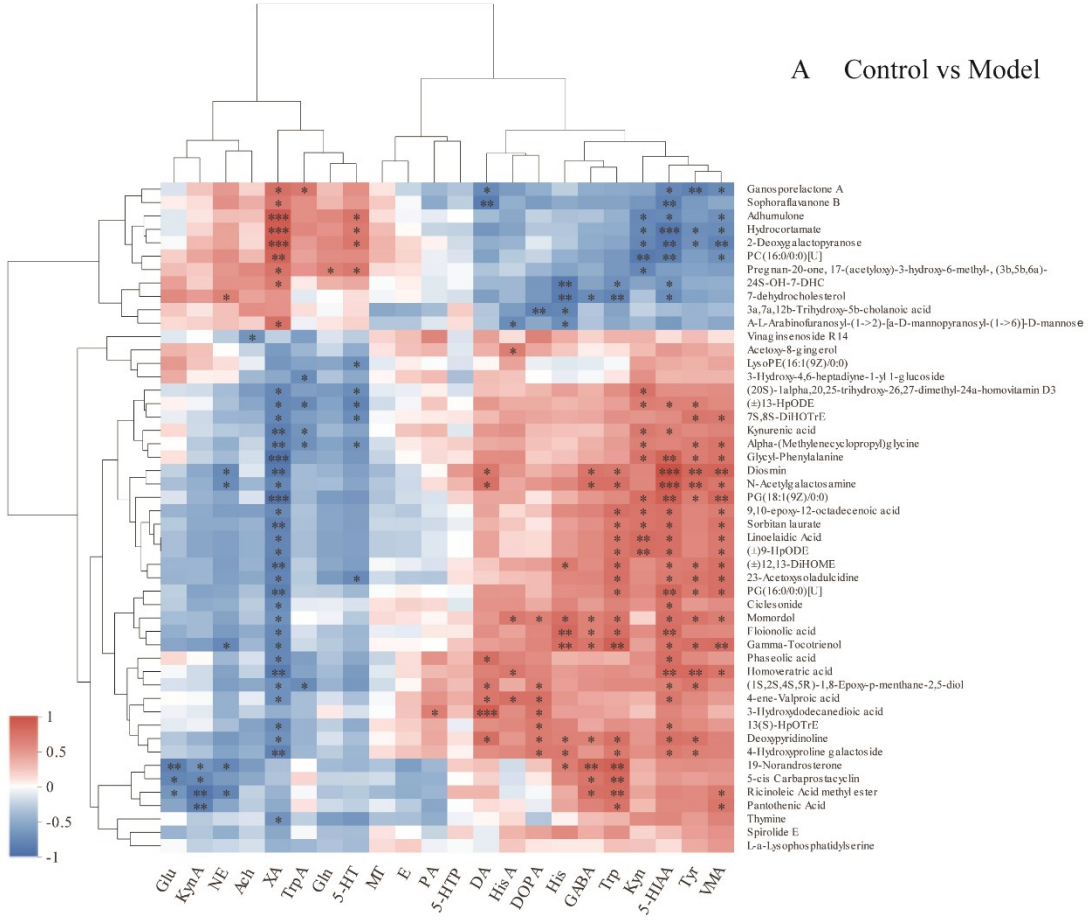

A Control vs Model
Ganosporelactone A
Sophoraflavanone B
Adhumulone
Hydrocortamate
2-Deoxygalactopyranose
PC(16:0/0:0)[U]
Pregnan-20-one, 17-(acetyloxy)-3-hydroxy-6-methyl-, (3b,5b,6a)-
24S-OH-7-DHC
7-dehydrocholesterol
3a,7a,12b-Trihydroxy-5b-cholanoic acid
A-L-Arabinofuranosyl-(1->2)-[a-D-mannopyranosyl-(1->6)]-D-mannose
Vinaginsenoside R14
Acetoxy-8-gingerol
LysoPE(16:1(9Z)/0:0)
3-Hydroxy-4,6-heptadiyne-1-yl 1-glucoside
(20S)-1alpha,20,25-trihydroxy-26,27-dimethyl-24a-homovitamin D3
(±)13-HpODE
7S,8S-DiHOTrE
Kynurenic acid
Alpha-(Methylenecyclopropyl)glycine
Glycyl-Phenylalanine
Diosmin
N-Acetylgalactosamine
PG(18:1(9Z)/0:0)
9,10-epoxy-12-octadecenoic acid
Sorbitan laurate
Linoelaidic Acid
(±)9-11pODE
(±)12,13-DiHOME
23-Acetoxysoladulcidine
PG(16:0/0:0)[U]
Ciclesonide
Momordol
Floionolic acid
Gamma-Tocotrienol
Phaseolic acid
Homoveratric acid
(1S,2S,4S,5R)-1,8-Epoxy-p-menthane-2,5-diol
4-ene-Valproic acid
3-Hydroxydodecanedioic acid
13(S)-HpOTrE
Deoxypyridinoline
4-Hydroxyproline galactoside
19-Norandrosterone
5-cis Carbaprostacyclin
Ricinoleic Acid methyl ester
Pantothenic Acid
Thymine
Spirolide E
L-a-lysophosphatidylserine
1
0.5
0
-0.5
-1
Glu
KynA
NE
Ach
XA
TrpA
Gln
5-HT
MT
E
PA
5-HTP
DA
His A
DOPA
His
GABA
Trp
Kyn
5-HIAA
Tyr
VMA

Figure S4 A

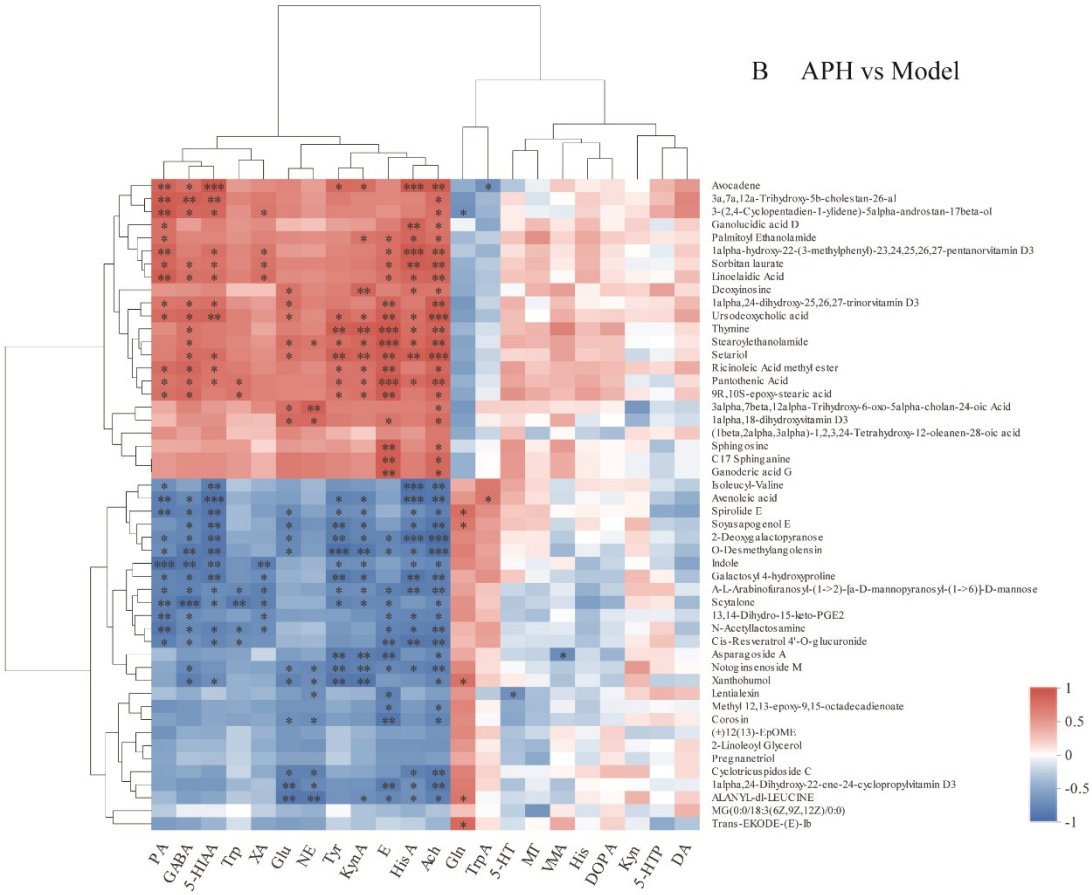

B APH vs Model
Avocadene
3a,7a,12a-Trihydroxy-5b-cholestan-26-al
3-(2,4-Cyclopentadien-1-ylidene)-5alpha-androstan-17beta-ol
Ganolucidic acid D
Palmitoyl Ethanolamide
1alpha-hydroxy-22-(3-methylphenyl)-23,24,25,26,27-pentanorvitamin D3
Sorbitan laurate
Linoelaidic Acid
Deoxyinosine
1alpha,24-dihydroxy-25,26,27-trinorvitamin D3
Ursodeoxycholic acid
Thymine
Stearoylethanolamide
Setariol
Ricinoleic Acid methyl ester
Pantothenic Acid
9R,10S-epoxy-stearic acid
3alpha,7beta,12alpha-Trihydroxy-6-oxo-5alpha-cholan-24-oic Acid
1alpha,18-dihydroxyvitamin D3
(1beta,2alpha,3alpha)-1,2,3,24-Tetrahydroxy-12-oleanen-28-oic acid
Sphingosine
C17 Sphinganine
Ganoderic acid G
Isoleucyl-Valine
Avenoleic acid
Spirolide E
Soyasapogenol E
2-Deoxygalactopyranose
O-Desmethylangolensin
Indole
Galactosyl 4-hydroxyproline
A-L-Arabinofuranosyl-(1->2)-[a-D-mannopyranosyl-(1->6)]-D-mannose
Scytalone
13,14-Dihydro-15-keto-PGE2
N-Acetyllactosamine
Cis-Resveratrol 4'-O-glucuronide
Asparagoside A
Notoginsenoside M
Xanthohumol
Lentialexin
Methyl 12,13-epoxy-9,15-octadecadienoate
Corosin
(+)12(13)-EpOME
2-Linoleoyl Glycerol
Pregnanetriol
Cyclotricuspidoside C
1alpha,24-Dihydroxy-22-ene-24-cyclopropylvitamin D3
ALANYL-dl-LEUCINE
MG(0:0/18:3(6Z,9Z,12Z)/0:0)
Trans-EKODE-(E)-Ib
1
0.5
0
-0.5
-1
PA
GABA
5-HIAA
Trp
XA
Glu
NE
Tyr
KynA
E
His.A
Ach
Gln
TrpA
5-HT
MT
VMA
His
DOPA
Kyn
5-HTP
DA

Figure S4 B

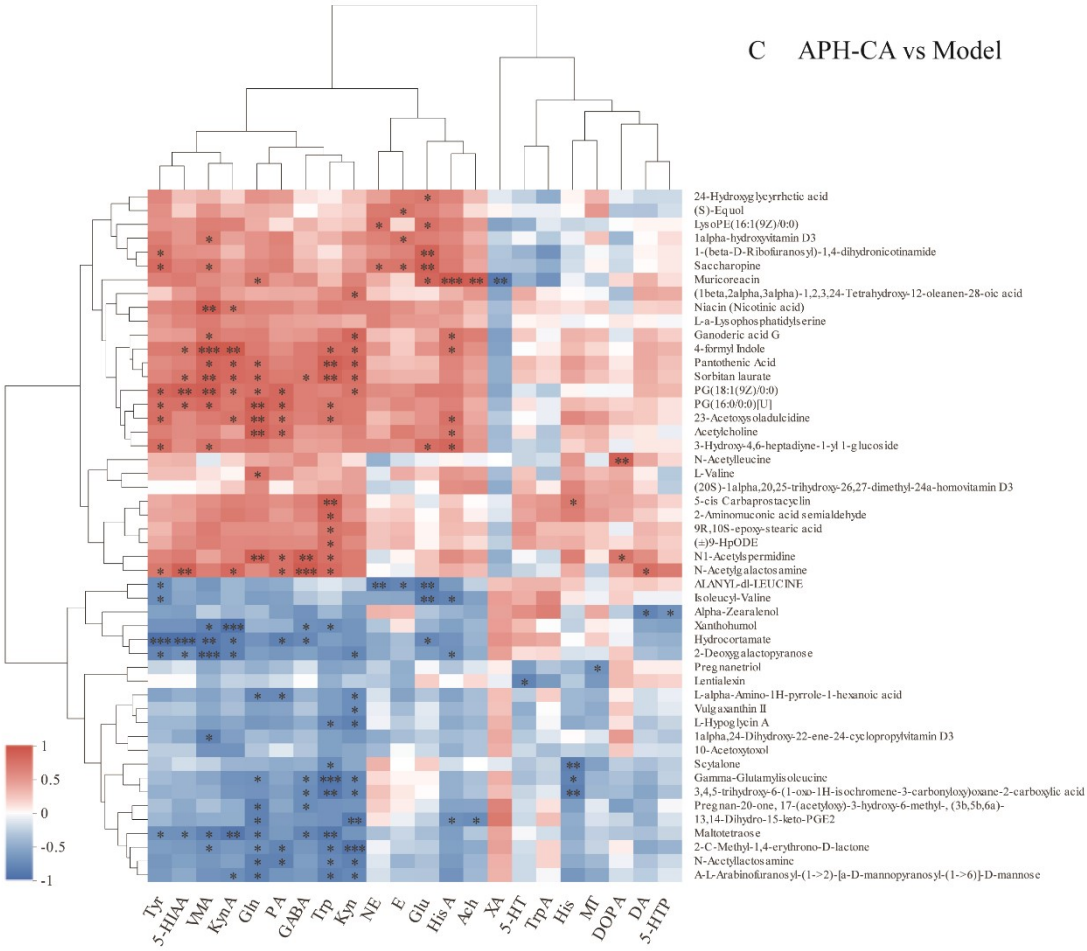

C APH-CA vs Model
24-Hydroxyglycyrrhetic acid
(S)-Equol
LysoPE(16:1(9Z)/0:0)
1alpha-hydroxyvitamin D3
1-(beta-D-Ribofuranosyl)-1,4-dihydronicotinamide
Saccharopine
Muricoreacin
(1beta,2alpha,3alpha)-1,2,3,24-Tetrahydroxy-12-oleanen-28-oic acid
Niacin (Nicotinic acid)
L-a-Lysophosphatidylserine
Ganoderic acid G
4-formyl Indole
Pantothenic Acid
Sorbitan laurate
PG(18:1(9Z)/0:0)
PG(16:0/0:0)[U]
23-Acetoxysoladulcidine
Acetylcholine
3-Hydroxy-4,6-heptadiyne-1-yl 1-glucoside
N-Acetylleucine
L-Valine
(20S)-1alpha,20,25-trihydroxy-26,27-dimethyl-24a-homovitamin D3
5-cis Carbaprostacyclin
2-Aminomuconic acid semialdehyde
9R,10S-epoxy-stearic acid
(±)9-HpODE
N1-Acetylspermidine
N-Acetylgalactosamine
ALANYL-dl-LEUCINE
Isoleucyl-Valine
Alpha-Zearalenol
Xanthohumol
Hydrocortamate
2-Deoxygalactopyranose
Pregnanetriol
Lentialexin
L-alpha-Amino-1H-pyrrole-1-hexanoic acid
Vulgaxanthin II
L-Hypoglycin A
1alpha,24-Dihydroxy-22-ene-24-cyclopropylvitamin D3
10-Acetoxytoxol
Scytalone
Gamma-Glutamylisoleucine
3,4,5-trihydroxy-6-(1-oxo-1H-isochromene-3-carbonyloxy)oxane-2-carboxylic acid
Pregnan-20-one, 17-(acetyloxy)-3-hydroxy-6-methyl-, (3b,5b,6a)-
13,14-Dihydro-15-keto-PGE2
Maltotetraose
2-C-Methyl-1,4-erythrono-D-lactone
N-Acetyllactosamine
A-L-Arabinofuranosyl-(1->2)-[a-D-mannopyranosyl-(1->6)]-D-mannose
1
0.5
0
-0.5
-1
Tyr
5-HIAA
VMA
Kyn.A
Gln
P.A
GABA
Trp
Kyn
NE
E
Glu
His.A
Ach
XA
5-HT
TrpA
His
MT
DOPA
DA
5-HTP

Figure S4 C

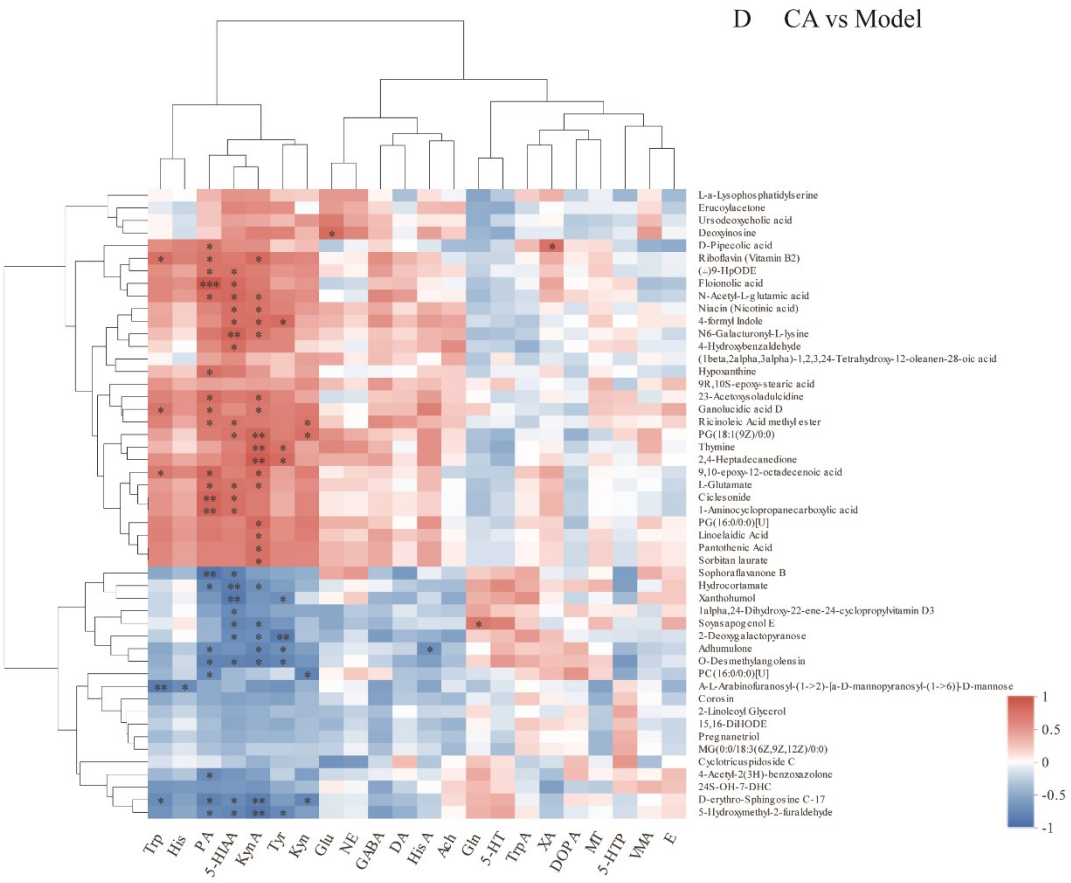

D CA vs Model
L-a-Lysophosphatidylserine
Erucoylacetone
Ursodeoxycholic acid
Deoxyinosine
D-Pipecolic acid
Riboflavin (Vitamin B2)
(-)9-HpODE
Floionolic acid
N-Acetyl-L-glutamic acid
Niacin (Nicotinic acid)
4-formyl Indole
N6-Galacturonyl-L-lysine
4-Hydroxybenzaldehyde
(1beta,2alpha,3alpha)-1,2,3,24-Tetrahydroxy-12-oleanen-28-oic acid
Hypoxanthine
9R,10S-epoxy-stearic acid
23-Acetoxysoladulcidine
Ganoluicidic acid D
Ricinoleic Acid methyl ester
PG(18:1(9Z)/0:0)
Thymine
2,4-Heptadecanedione
9,10-epoxy-12-octadecenoic acid
L-Glutamate
Ciclesonide
1-Aminocyclopropanecarboxylic acid
PG(16:0/0:0)[U]
Linoelaidic Acid
Pantothenic Acid
Sorbitan laurate
Sophoraflavanone B
Hydrocortamate
Xanthohumol
1alpha,24-Dihydroxy-22-ene-24-cyclopropylvitamin D3
Soyasapogenol E
2-Deoxygalactopyranose
Adhumulone
O-Desmethylangolensin
PC(16:0/0:0)[U]
A-L-Arabinofuranosyl-(1->2)-[a-D-mannopyranosyl-(1->6)]-D-mannose
Corosin
2-Linoleoyl Glycerol
15,16-DiHODE
Pregnanetriol
MG(0:0/18:3(6Z,9Z,12Z)/0:0)
Cyclotricuspidoside C
4-Acetyl-2(3H)-benzoxazolone
24S-OH-7-DHC
D-erythro-Sphingosine C-17
5-Hydroxymethyl-2-furaldehyde
Trp
His
PA
5-HIAA
Kyn A
Tyr
Kyn
Glu
NE
GABA
DA
His A
Ach
Gln
5-HT
Trp A
XA
DOPA
MT
5-HTP
VMA
E
1
0.5
0
-0.5
-1

Figure S4 D

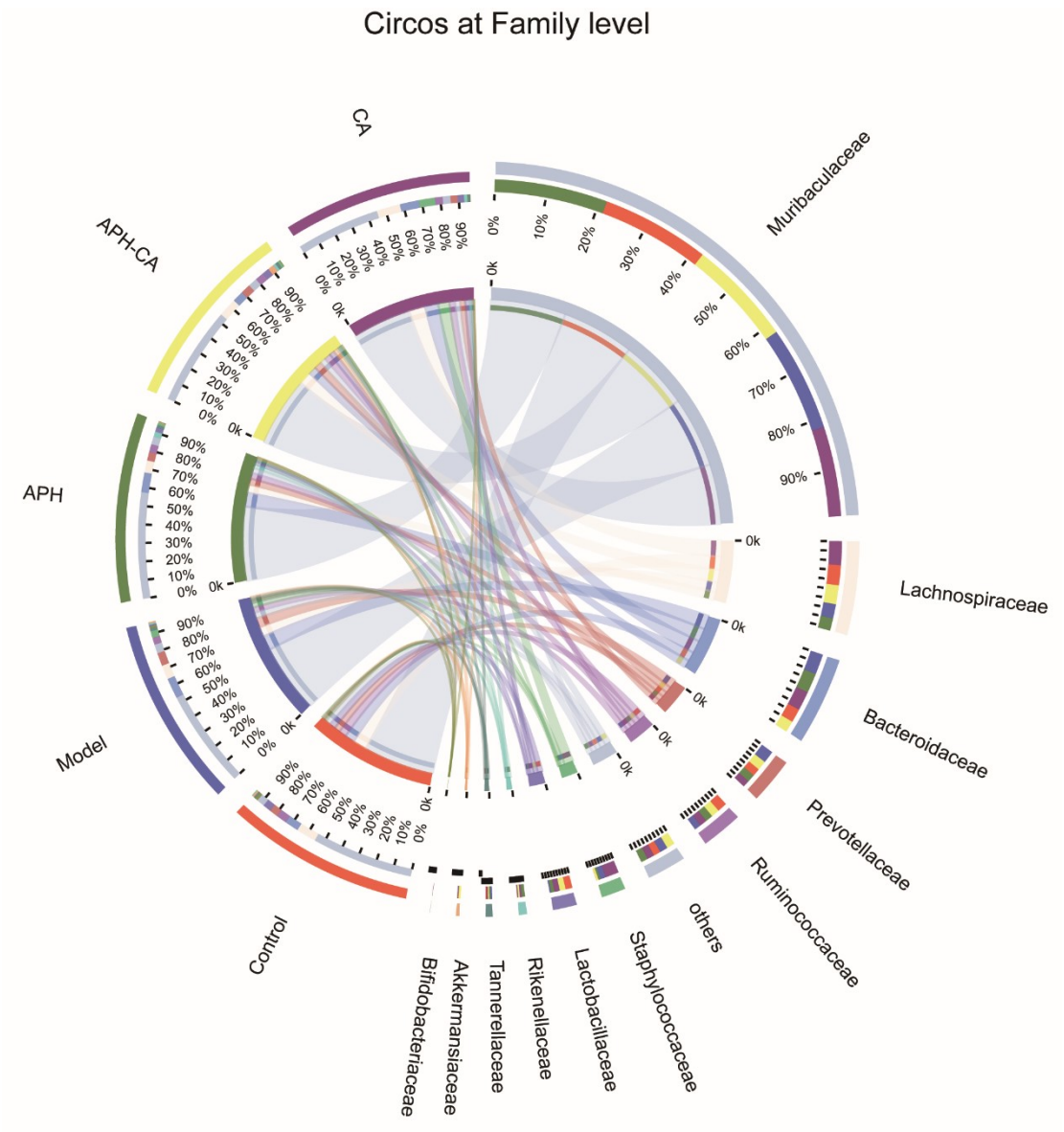

Circos at Family level
CA
APH-CA
APH
Model
Control
Muribaculaceae
Lachnospiraceae
Bacteroidaceae
Prevotellaceae
Ruminococcaceae
others
Staphylococcaceae
Lactobacillaceae
Rikenellaceae
Tannerellaceae
Akkermansiaceae
Bifidobacteriaceae

Figure S5

Table S1 α diversity index table

Sample\Estimators	sobs	shannon	ace	chao	shannoneven
control	538.83 ±18.28	4.41±0.22	620.93±22.48	625.24±21.27	0.7±0.03
model	510.33±51.55	4.26±0.28	592.91±38.84	593.42±39.55	0.68±0.04
APH	446.15±196.02	3.67±1.67	512.47±234.72	509.98±234.03	0.58±0.27
APH-CA	540.00±29.28	4.40±0.18	619.49±45.78	635.11±51.55	0.70±0.03
CA	464.50±55.07	3.97±0.48	556.05±40.33	557.70±55.60	0.65±0.07