高脂肪饮食对妊娠小鼠及其后代肝脏健康的影响：肠-肝轴的作用

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Qian Gong, Yufei Zhang, Juxiong Liu, Shuai Yuan, Huijie Hu, Yu Cao, Shoupeng Fu, et al. 2025. ".The Impact of a High-Fat Diet on Liver Health in Pregnant Mice and Their Offspring: The Role of the Gut-Liver Axis".
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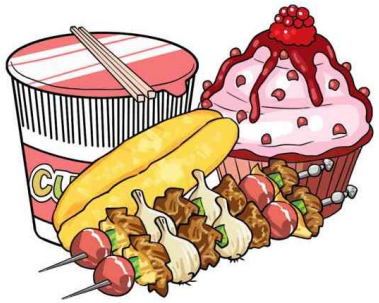
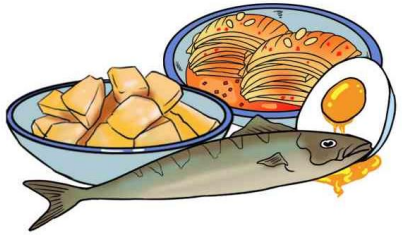
研究背景

高脂饮食（High-fat diet, HFD）与脂肪肝疾病的关联

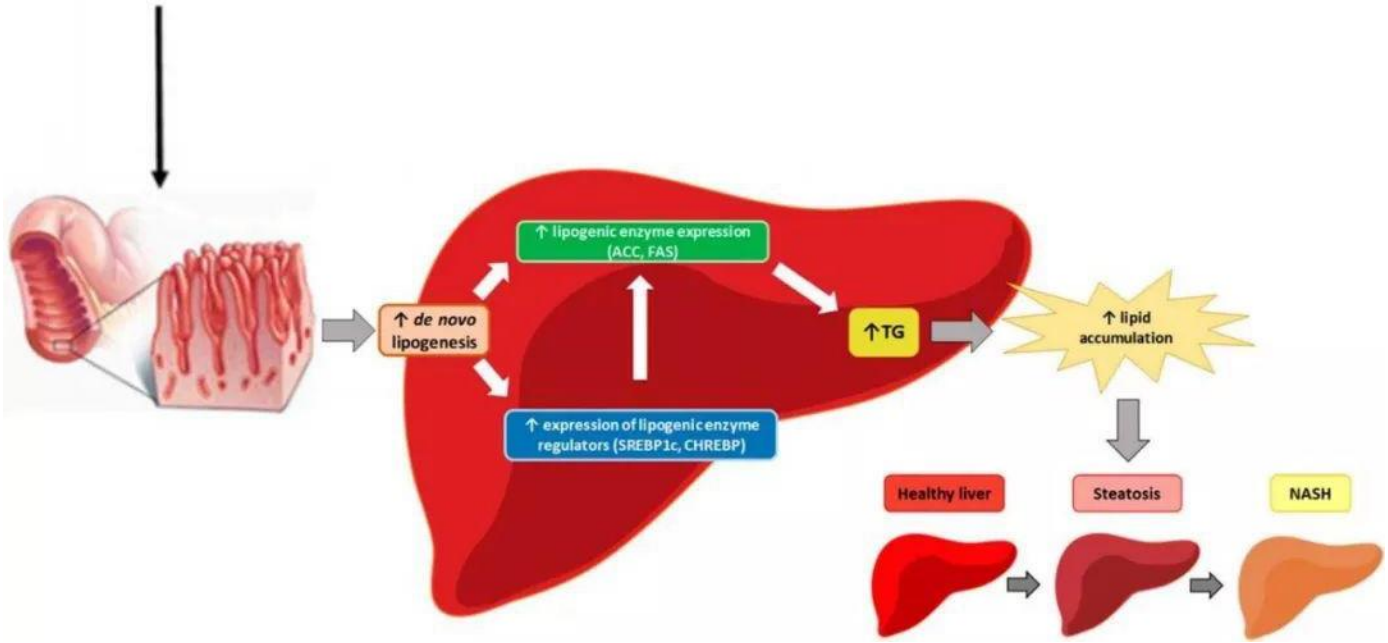
高糖食物



高脂食物



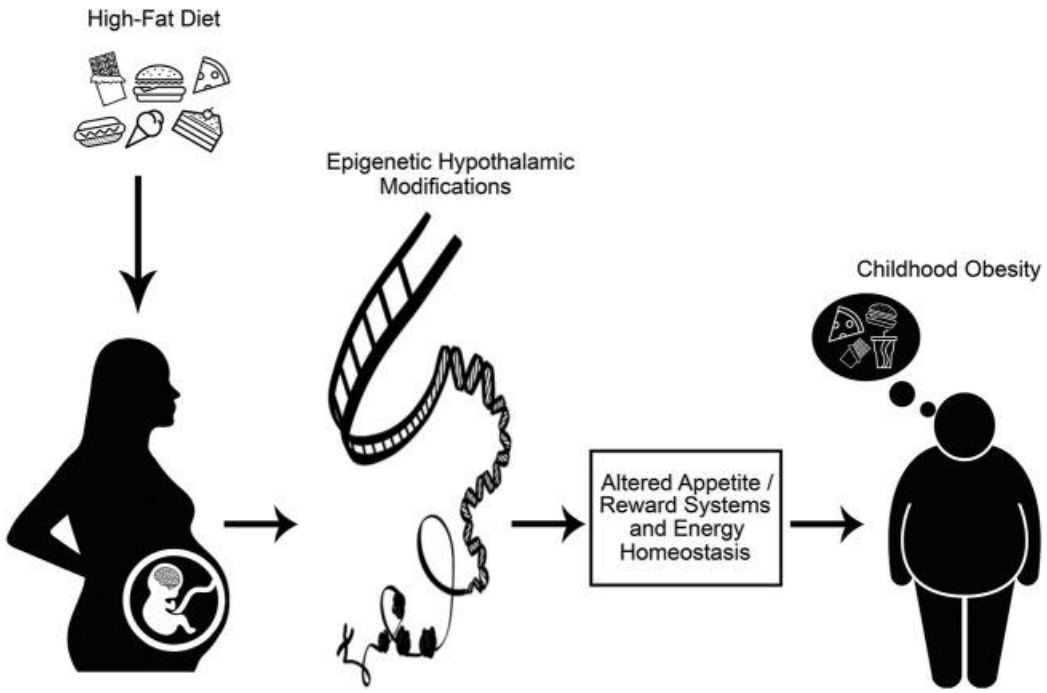
高盐食物



- 肝脏作为人体的“代谢中枢”，是HFD攻击的首要目标。
- 脂质在肝细胞内堆积，形成脂肪滴，逐渐发展为脂肪肝。
- 脂肪堆积导致氧化应激增强，线粒体功能受损，炎症因子（如TNF-α、IL-6）大量释放，形成恶性循环。
- 孕期女性的代谢系统会发生剧烈变化（如雌激素水平激增、胰岛素敏感性下降），这使得HFD对肝脏的影响可能被放大。

研究背景

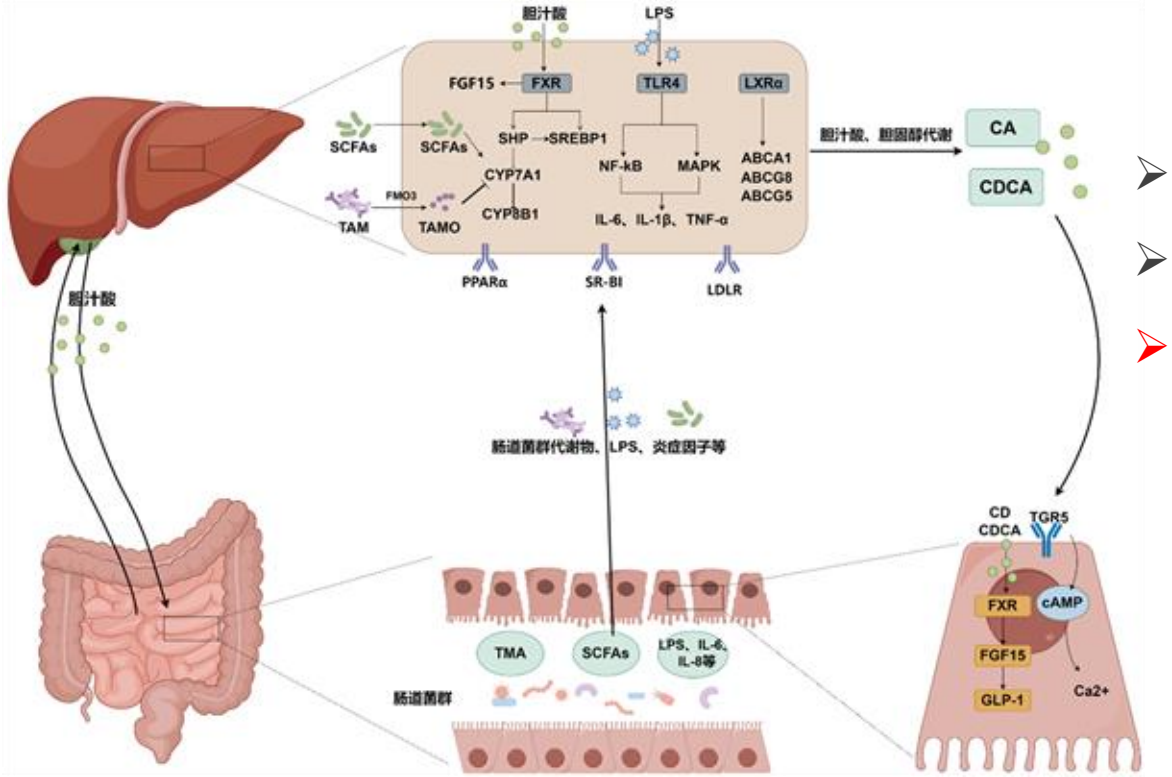
孕期HFD对母体及后代的双重影响



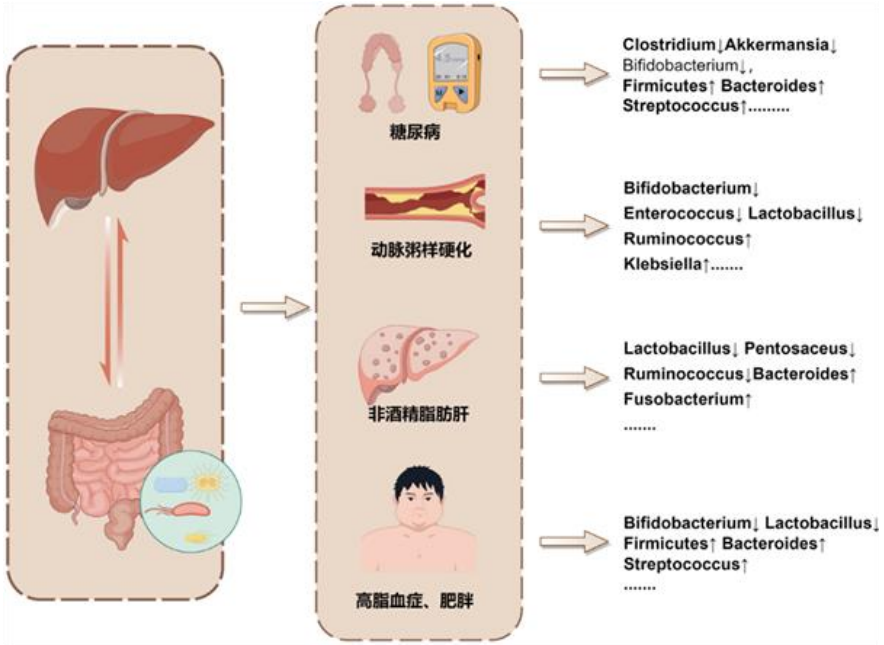
- 全球约35%的孕妇存在HFD摄入过量问题，导致孕期脂肪肝发病率高达18%。
- 母体的代谢紊乱会通过“代谢记忆”传递给子代。
- 母体肝脏释放的损伤相关分子模式（DAMPs）可通过胎盘屏障，激活胎儿肝脏的Kupffer细胞，引发子代肝脏的慢性炎症。
- 孕期HFD可能通过“母体肝损伤-胎盘信号传递-子代肝脏编程”的三级联反应影响后代。然而，这一假说尚未被实验验证。

研究背景

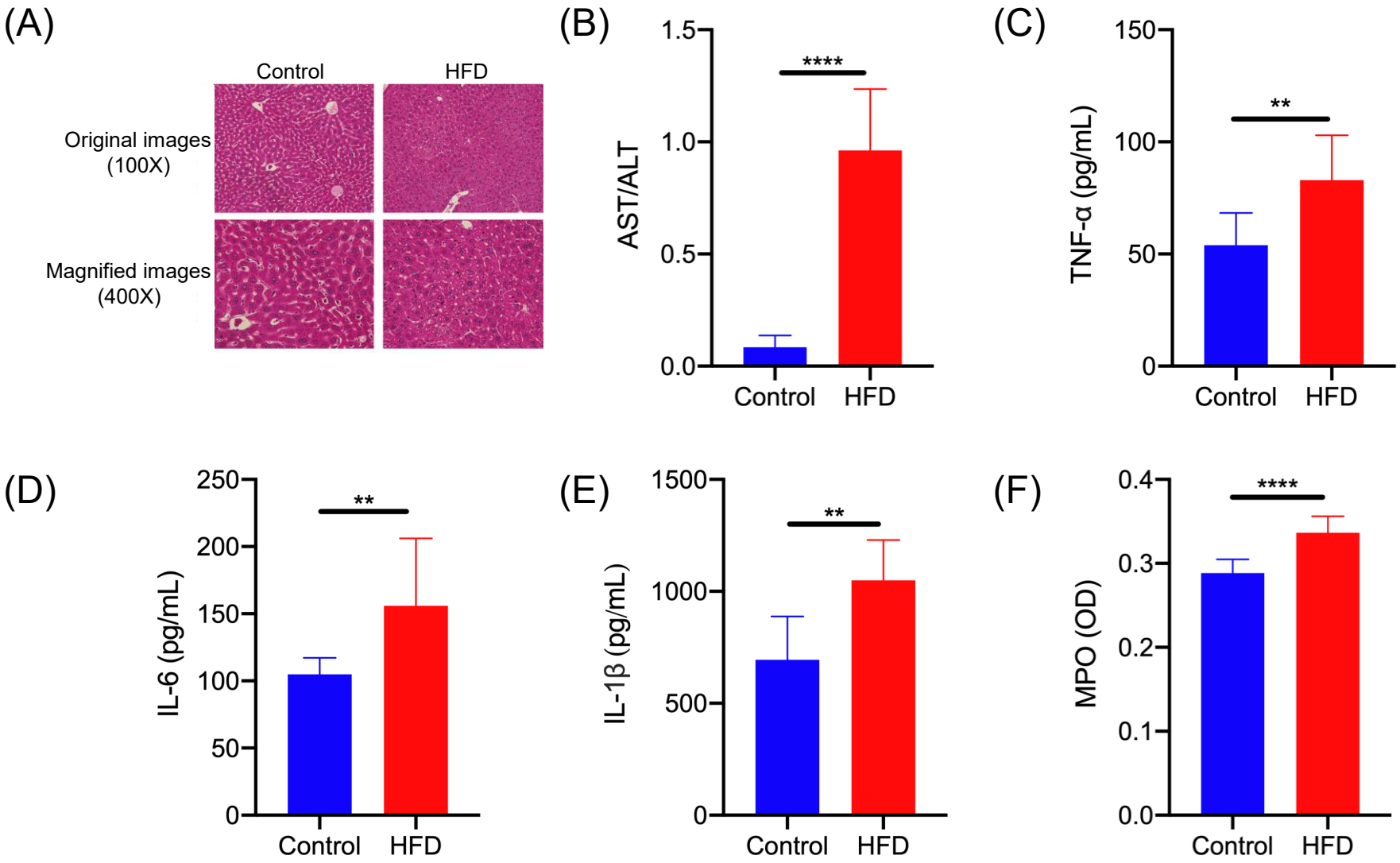
肠道菌群在代谢中的核心作用



- 肠道菌群堪称人体的“隐形器官”，其代谢能力远超肝脏。通过肠肝轴（gut-liver axis），菌群与肝脏进行着密集的“分子对话”。
- 当饮食中脂肪比例超过40%时，胆汁酸分泌模式改变。
- 孕期的特殊性进一步放大了菌群的作用。
- 孕期HFD如何通过菌群影响母体肝脏？是否传递给子代？

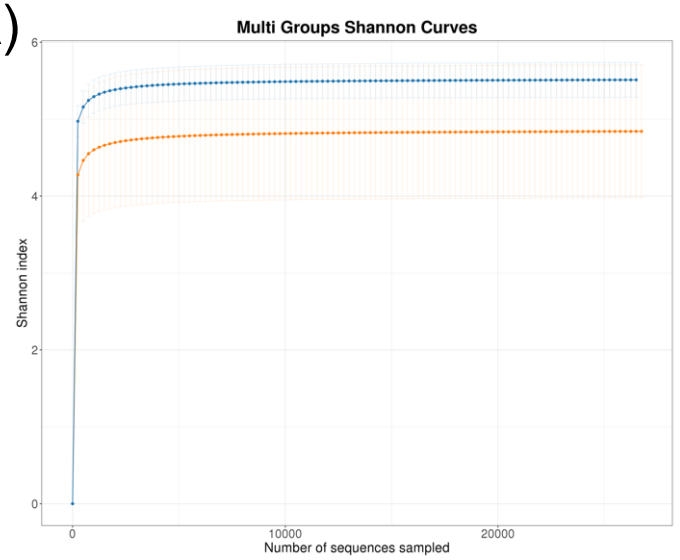


正文

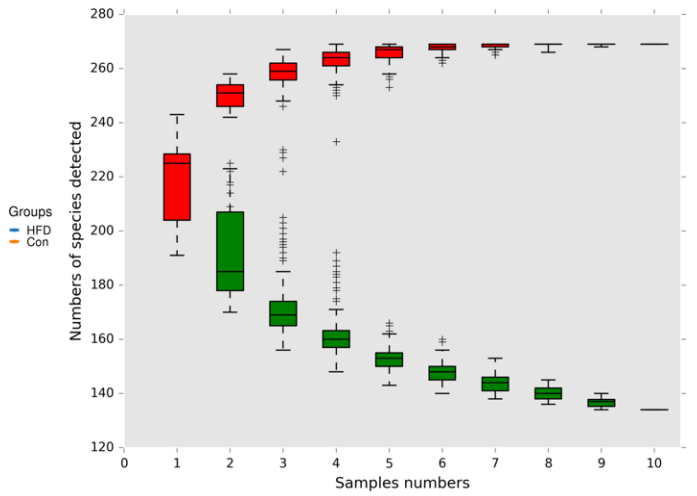

(A)
Control
HFD
Original images (100X)
Magnified images (400X)
(B)
AST/ALT
1.5
1.0
0.5
0.0
****
Control
HFD
(C)
TNF-α (pg/mL)
150
100
50
0
**
Control
HFD
(D)
IL-6 (pg/mL)
250
200
150
100
50
0
**
Control
HFD
(E)
IL-1β (pg/mL)
1500
1000
500
0
**
Control
HFD
(F)
MPO (OD)
0.4
0.3
0.2
0.1
0.0
****
Control
HFD

正文

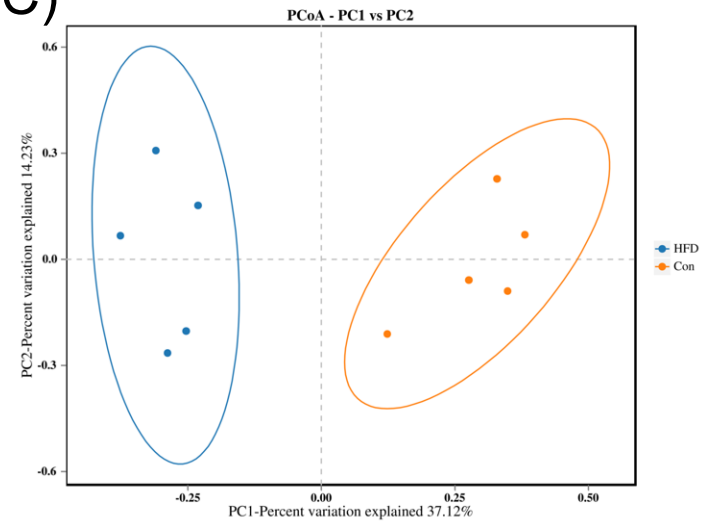
(A)


Multi Groups Shannon Curves
Shannon index
Number of sequences sampled
0
2
4
6
0
10000
20000

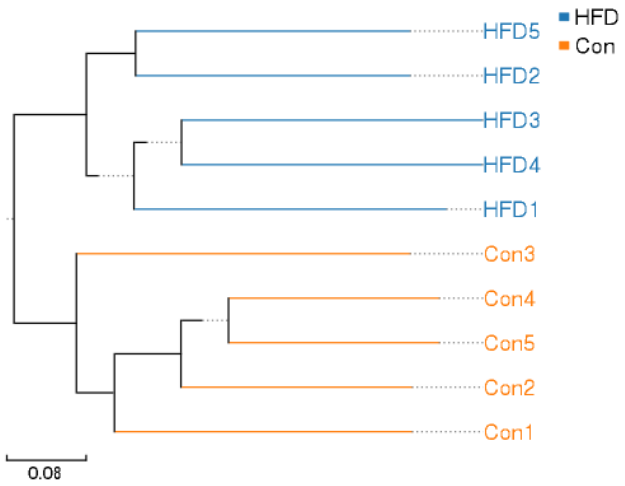
(B)


Numbers of species detected
Samples numbers
Groups
HFD
Con
120
140
160
180
200
220
240
260
280
0
1
2
3
4
5
6
7
8
9
10

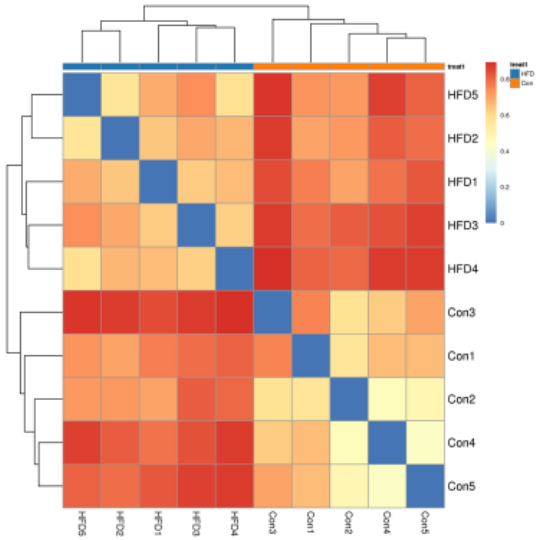
(C)


PCoA - PC1 vs PC2
PC2-Percent variation explained 14.23%
PC1-Percent variation explained 37.12%
HFD
Con
0.6
0.3
0.0
-0.3
-0.6
-0.25
0.00
0.25
0.50

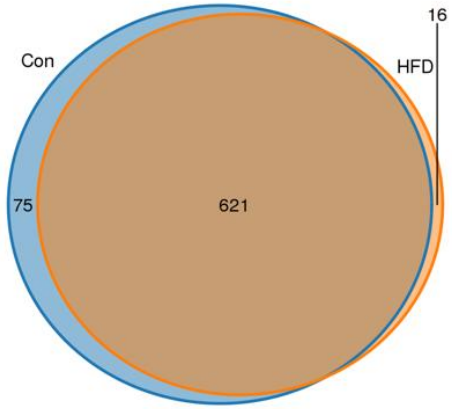
(D)


HFD
Con
HFD5
HFD2
HFD3
HFD4
HFD1
Con3
Con4
Con5
Con2
Con1
0.08

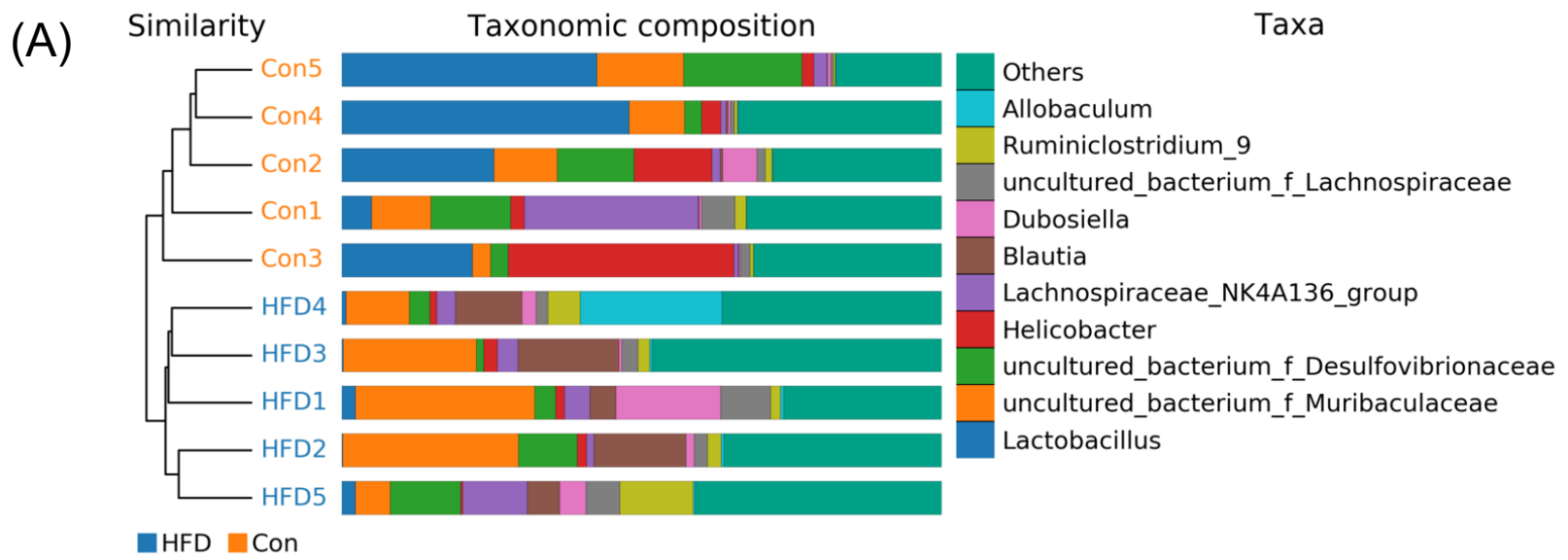
(E)

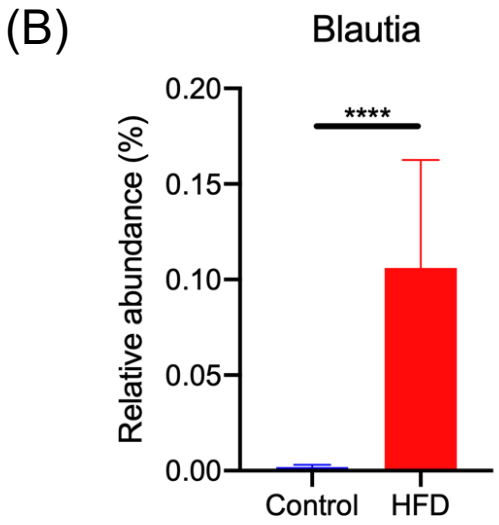

HFD5
HFD2
HFD1
HFD3
HFD4
Con3
Con1
Con2
Con4
Con5

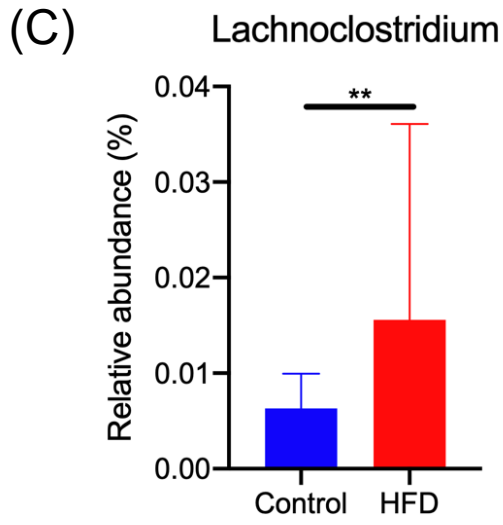
(F)

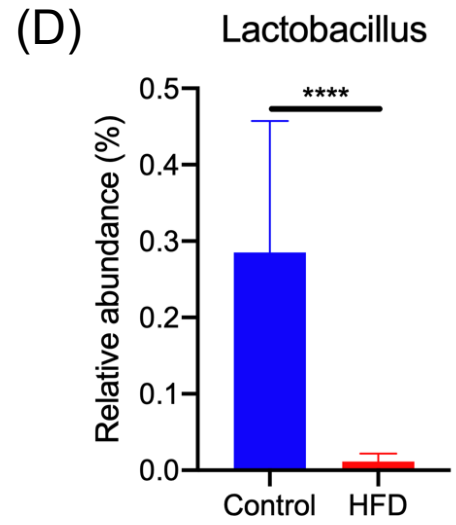

Con
HFD
16
75
621

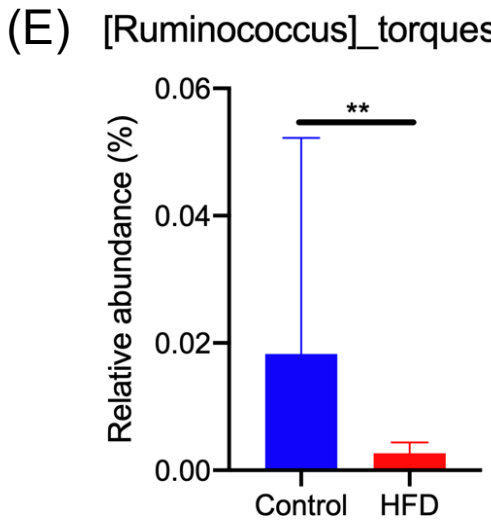
正文

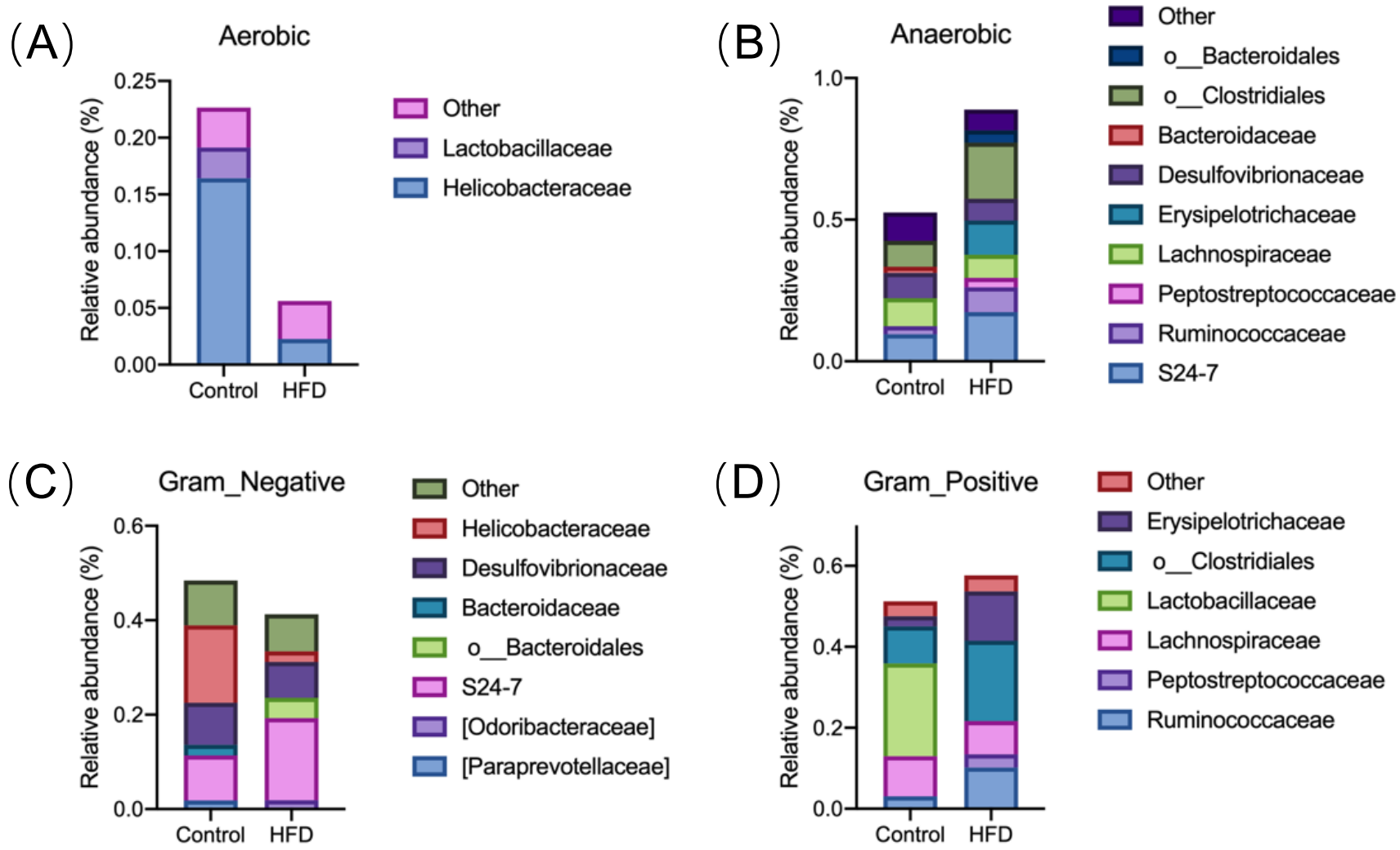

(A)
Similarity
Taxonomic composition
Taxa
Con5
Con4
Con2
Con1
Con3
HFD4
HFD3
HFD1
HFD2
HFD5
HFD
Con
Others
Allobaculum
Ruminiclostridium_9
uncultured_bacterium_f_Lachnospiraceae
Dubosiella
Blautia
Lachnospiraceae_NK4A136_group
Helicobacter
uncultured_bacterium_f_Desulfovibrionaceae
uncultured_bacterium_f_Muribaculaceae
Lactobacillus


(B)
Blautia
Relative abundance (%)
0.20
0.15
0.10
0.05
0.00
****
Control
HFD

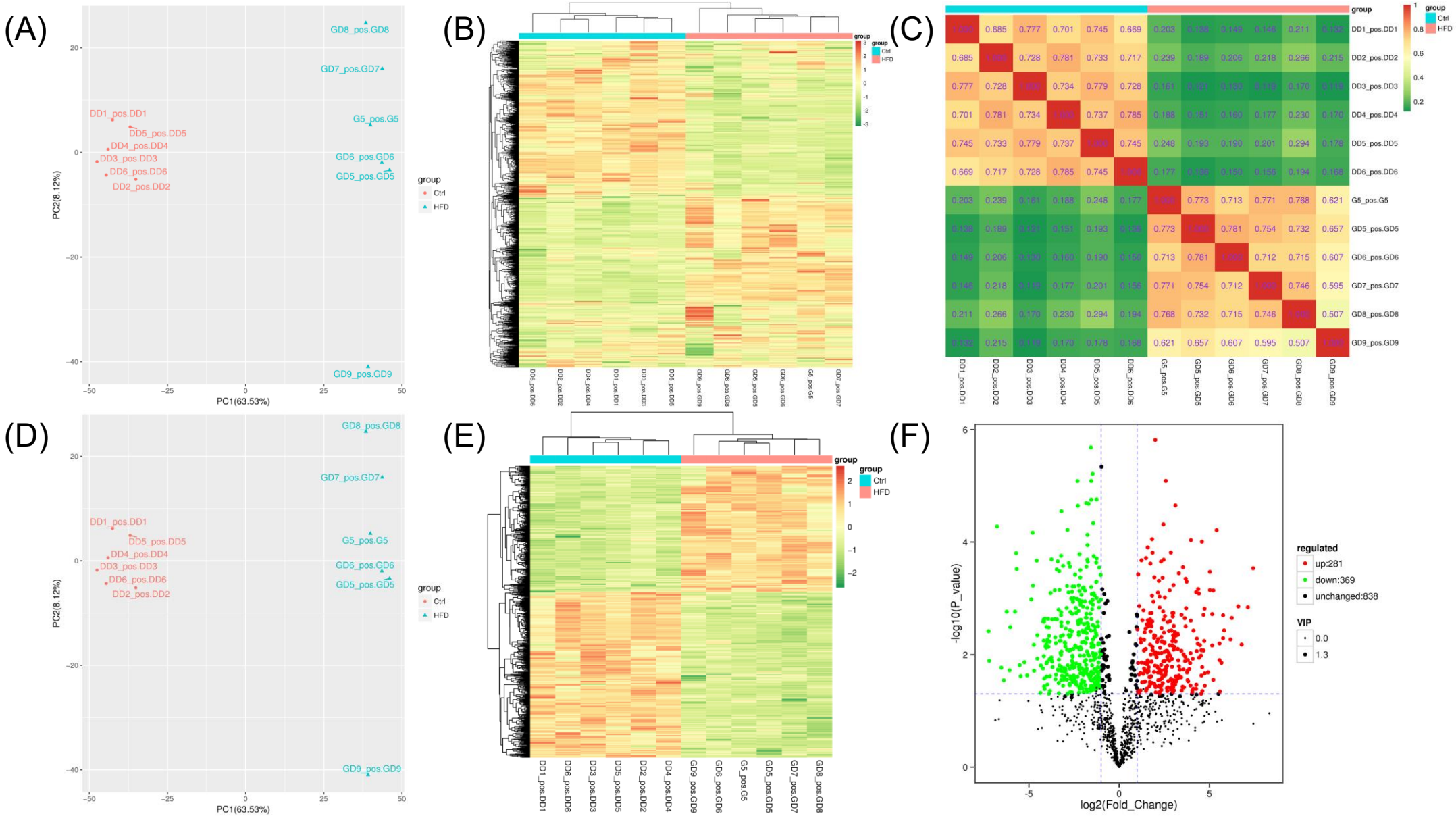

(C)
Lachnoclostridium
Relative abundance (%)
0.04
0.03
0.02
0.01
0.00
**
Control
HFD


(D)
Lactobacillus
Relative abundance (%)
0.5
0.4
0.3
0.2
0.1
0.0
****
Control
HFD


(E)
[Ruminococcus]_torques_group
Relative abundance (%)
0.06
0.04
0.02
0.00
**
Control
HFD

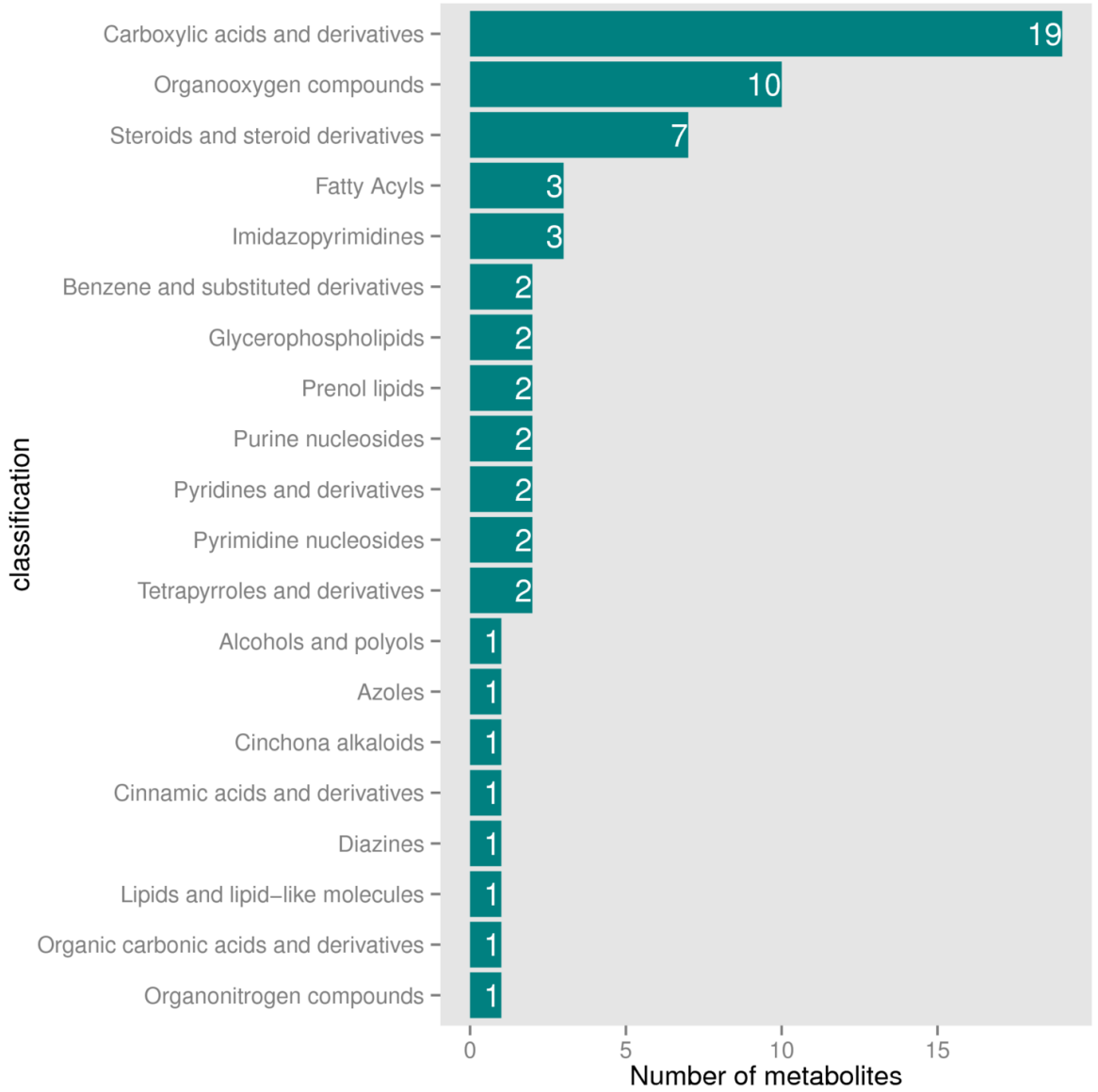

(A)
Aerobic
Relative abundance (%)
0.25
0.20
0.15
0.10
0.05
0.00
Control
HFD
Other
Lactobacillaceae
Helicobacteraceae
(B)
Anaerobic
Relative abundance (%)
1.0
0.5
0.0
Control
HFD
Other
o__Bacteroidales
o__Clostridiales
Bacteroidaceae
Desulfovibrionaceae
Erysipelotrichaceae
Lachnospiraceae
Peptostreptococcaceae
Ruminococcaceae
S24-7
(C)
Gram_Negative
Relative abundance (%)
0.6
0.4
0.2
0.0
Control
HFD
Other
Helicobacteraceae
Desulfovibrionaceae
Bacteroidaceae
o__Bacteroidales
S24-7
[Odoribacteraceae]
[Paraprevotellaceae]
(D)
Gram_Positive
Relative abundance (%)
0.6
0.4
0.2
0.0
Control
HFD
Other
Erysipelotrichaceae
o__Clostridiales
Lactobacillaceae
Lachnospiraceae
Peptostreptococcaceae
Ruminococcaceae

正文


(A)
GD8_pos.GD8
GD7_pos.GD7
DD1_pos.DD1
G5_pos.G5
DD5_pos.DD5
DD4_pos.DD4
DD3_pos.DD3
GD6_pos.GD6
DD6_pos.DD6
GD5_pos.GD5
DD2_pos.DD2
GD9_pos.GD9
PC2(8.12%)
PC1(63.53%)
group
Ctrl
HFD
(B)
group
Ctrl
HFD
(C)
group
Ctrl
HFD
DD1_pos.DD1
DD2_pos.DD2
DD3_pos.DD3
DD4_pos.DD4
DD5_pos.DD5
DD6_pos.DD6
G5_pos.G5
GD5_pos.GD5
GD6_pos.GD6
GD7_pos.GD7
GD8_pos.GD8
GD9_pos.GD9
(D)
GD8_pos.GD8
GD7_pos.GD7
DD1_pos.DD1
G5_pos.G5
DD5_pos.DD5
DD4_pos.DD4
DD3_pos.DD3
GD6_pos.GD6
DD6_pos.DD6
GD5_pos.GD5
DD2_pos.DD2
GD9_pos.GD9
PC2(8.12%)
PC1(63.53%)
group
Ctrl
HFD
(E)
group
Ctrl
HFD
(F)
-log10(P_value)
log2(Fold_Change)
regulated
up:281
down:369
unchanged:838
VIP
0.0
1.3

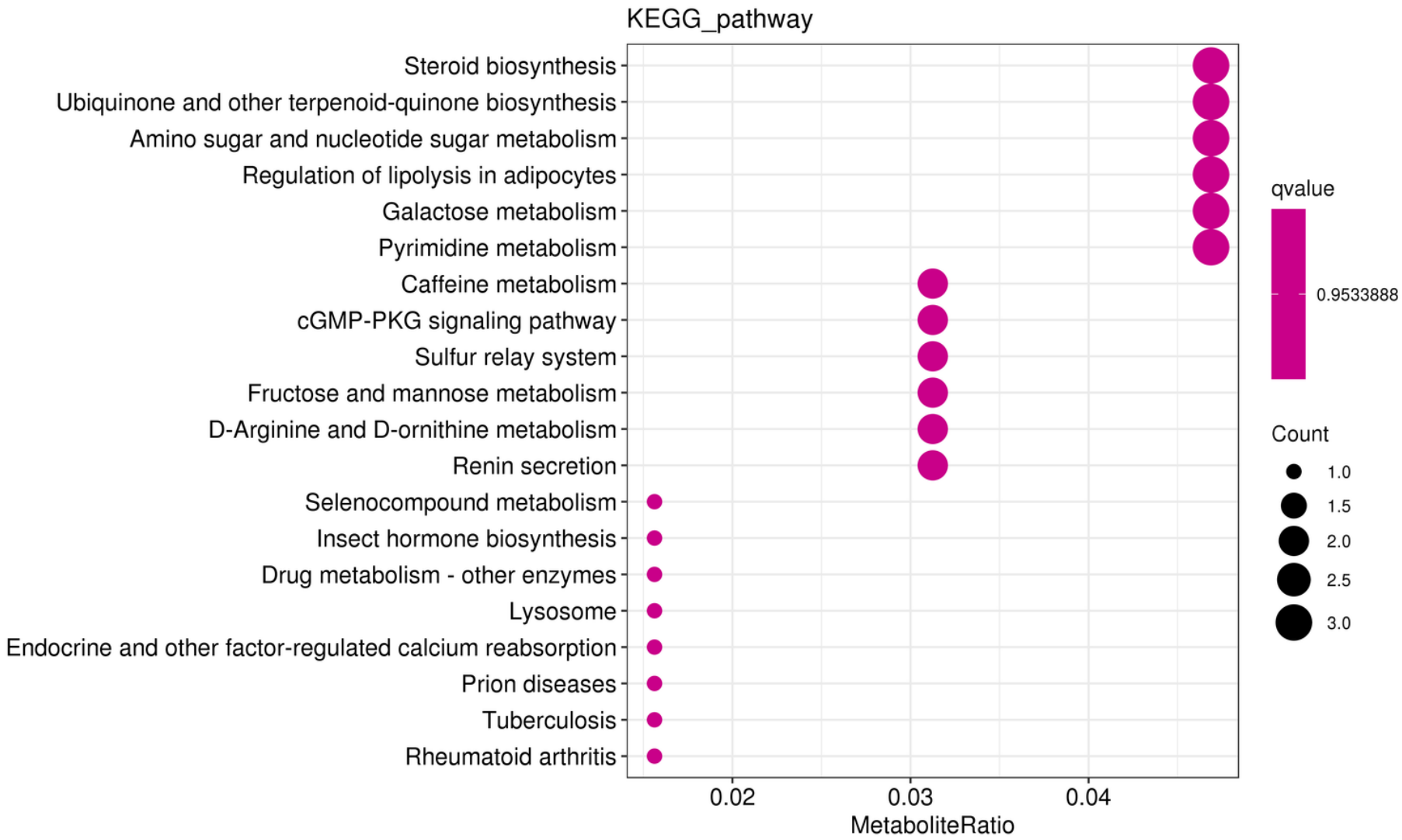
正文

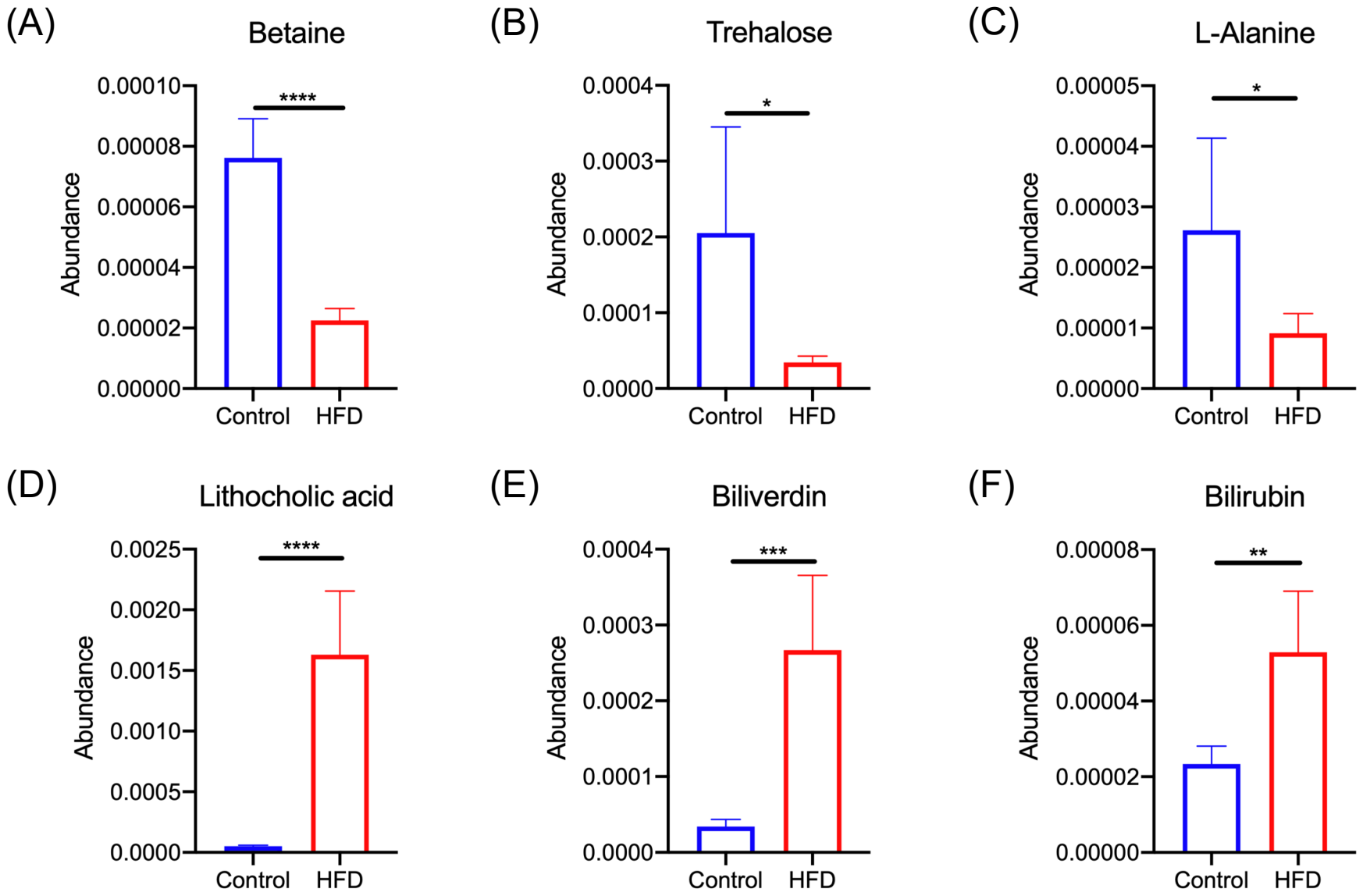
(G)

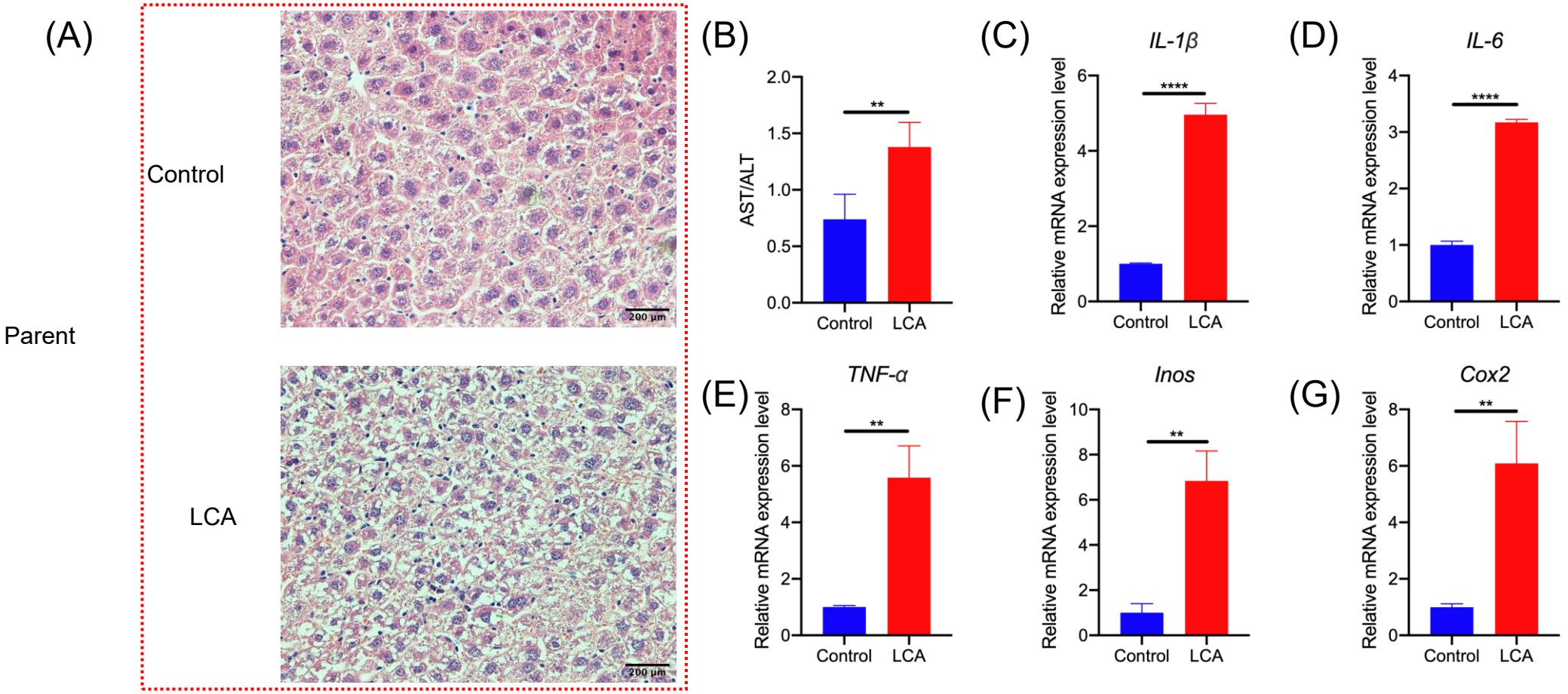


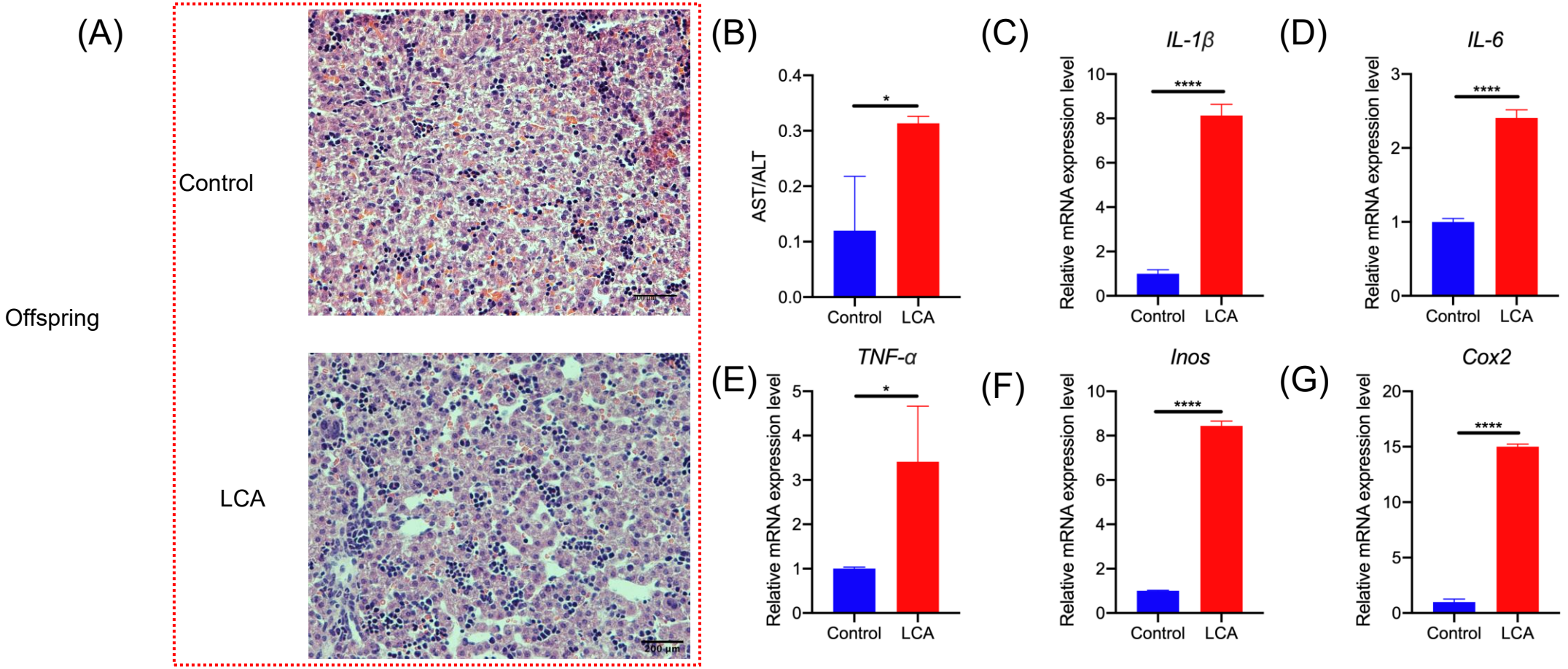
羧酸及其衍生物
含氧有机化合物
类固醇及其衍生物
脂肪胺基
咪唑嘧啶类

(H)

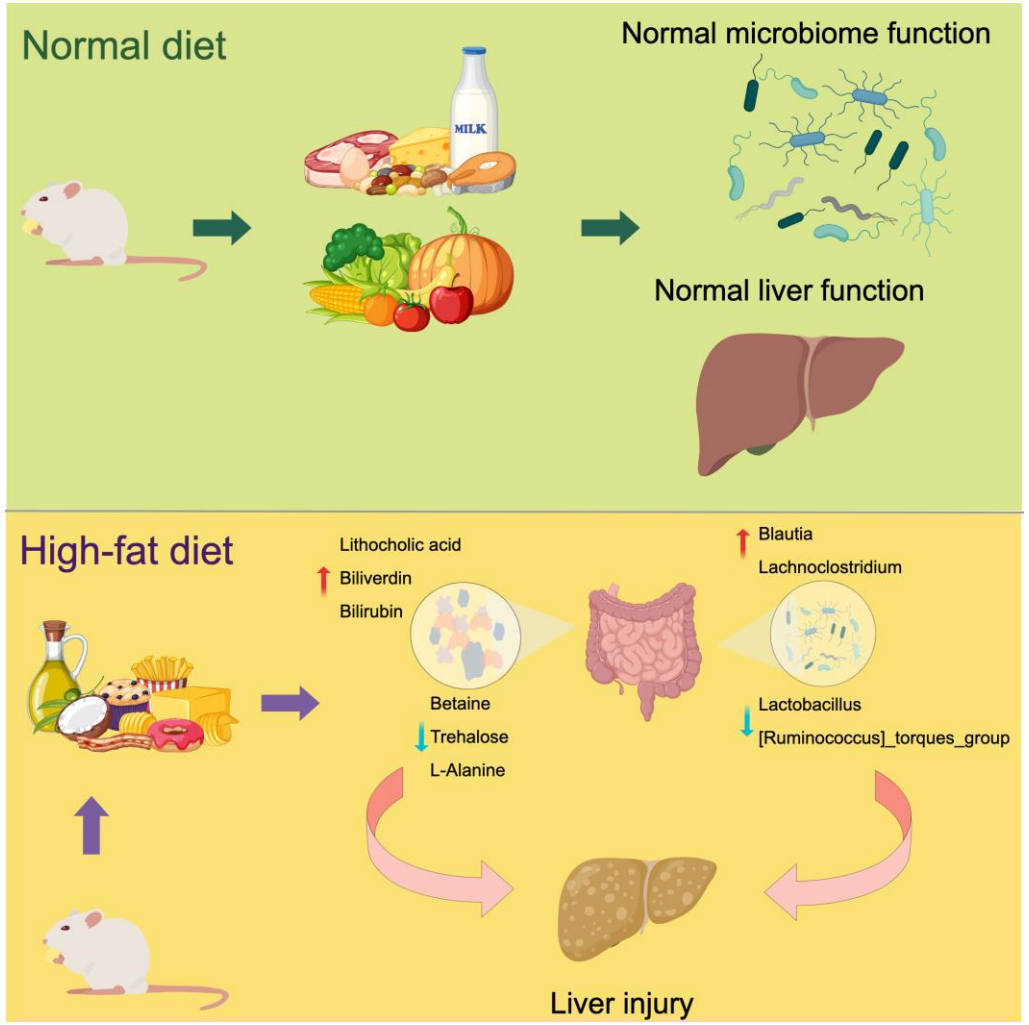

KEGG_pathway
Steroid biosynthesis
Ubiquinone and other terpenoid-quinone biosynthesis
Amino sugar and nucleotide sugar metabolism
Regulation of lipolysis in adipocytes
Galactose metabolism
Pyrimidine metabolism
Caffeine metabolism
cGMP-PKG signaling pathway
Sulfur relay system
Fructose and mannose metabolism
D-Arginine and D-ornithine metabolism
Renin secretion
Selenocompound metabolism
Insect hormone biosynthesis
Drug metabolism - other enzymes
Lysosome
Endocrine and other factor-regulated calcium reabsorption
Prion diseases
Tuberculosis
Rheumatoid arthritis
0.02
0.03
0.04
MetaboliteRatio
qvalue
0.9533888
Count
1.0
1.5
2.0
2.5
3.0


(A)
Betaine
0.00010
0.00008
0.00006
0.00004
0.00002
0.00000
Abundance
****
Control
HFD
(B)
Trehalose
0.0004
0.0003
0.0002
0.0001
0.0000
Abundance
*
Control
HFD
(C)
L-Alanine
0.00005
0.00004
0.00003
0.00002
0.00001
0.00000
Abundance
*
Control
HFD
(D)
Lithocholic acid
0.0025
0.0020
0.0015
0.0010
0.0005
0.0000
Abundance
****
Control
HFD
(E)
Biliverdin
0.0004
0.0003
0.0002
0.0001
0.0000
Abundance
***
Control
HFD
(F)
Bilirubin
0.00008
0.00006
0.00004
0.00002
0.00000
Abundance
**
Control
HFD


(A)
Control
Parent
LCA
200 μm
200 μm
(B)
AST/ALT
2.0
1.5
1.0
0.5
0.0
**
Control
LCA
(C)
IL-1β
Relative mRNA expression level
6
4
2
0
****
Control
LCA
(D)
IL-6
Relative mRNA expression level
4
3
2
1
0
****
Control
LCA
(E)
TNF-α
Relative mRNA expression level
8
6
4
2
0
**
Control
LCA
(F)
Inos
Relative mRNA expression level
10
8
6
4
2
0
**
Control
LCA
(G)
Cox2
Relative mRNA expression level
8
6
4
2
0
**
Control
LCA


(A)
Control
LCA
Offspring
200 μm
(B)
AST/ALT
0.4
0.3
0.2
0.1
0.0
*
Control
LCA
(C)
IL-1β
Relative mRNA expression level
10
8
6
4
2
0
****
Control
LCA
(D)
IL-6
Relative mRNA expression level
3
2
1
0
****
Control
LCA
(E)
TNF-α
Relative mRNA expression level
5
4
3
2
1
0
*
Control
LCA
(F)
Inos
Relative mRNA expression level
10
8
6
4
2
0
****
Control
LCA
(G)
Cox2
Relative mRNA expression level
20
15
10
5
0
****
Control
LCA

总结



- 妊娠期高脂肪饮食诱发肝脂肪变性；
- 怀孕期间的高脂肪饮食会导致肠道微生物群的改变和代谢紊乱；
- 妊娠期高脂肪饮食会破坏肠道代谢产物，如石胆酸（LCA）；
- 高脂饮食中LCA的改变会引起妊娠小鼠及其后代的肝脏炎症。

Qian Gong, Yufei Zhang, Juxiong Liu, Shuai Yuan, Huijie Hu, Yu Cao, Shoupeng Fu, et al. 2025. ".The Impact of a High-Fat Diet on Liver Health in Pregnant Mice and Their Offspring: The Role of the Gut-Liver Axis". ***iMetaOmics*** 2: e70026. https://doi.org/10.1002/imo2.70026

iMeta: 整合宏组学重新认识生物/医学/环境

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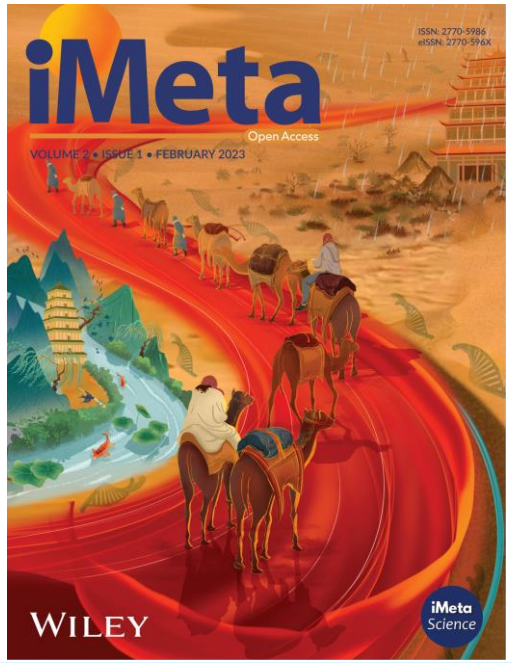

iMeta期刊(影响因子**23.8**)由宏科学、千名华人科学家和威立出版，主编刘双江和傅静远教授。目标为生物/医学/环境综合期刊群(对标Cell/Nature/Science)，任何高影响力的研究、方法和综述均欢迎投稿，重点关注技术、信息和组学等前沿交叉学科，已被SCIE、PubMed等收录，IF 23.8位列全球SCI期刊前千分之五，微生物学研究类全球第一，中科院生物学双1区Top；外审平均21天，投稿至发表中位数57天。

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