The Impact of a High-Fat Diet on Liver Health in Pregnant Mice and Their Offspring: The Role of the Gut-Liver Axis

Qian Gong[#1, 3], Yufei Zhang[#1], Juxiong Liu[1], Shuai Yuan[1], Huijie Hu[1], Yu Cao[1], Shoupeng Fu[1*] and Wenjin Guo[1, 2*]

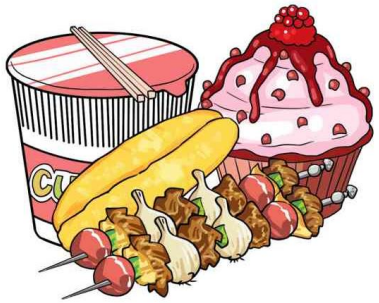
1. State Key Laboratory for Diagnosis and Treatment of Severe Zoonotic Infectious Diseases, Key Laboratory for Zoonosis Research of the Ministry of Education, Institute of Zoonosis, and College of Veterinary Medicine, Jilin University, ChangchunChina
2. Chongqing Research Institute, Jilin University, Chongqing, 401120, China
3. Department of Veterinary Medicine, College of Animal Sciences, Zhejiang University, Hangzhou, China

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

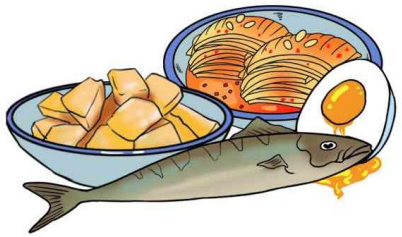
Introduction

The association between High-fat diet (HFD) and fatty liver disease

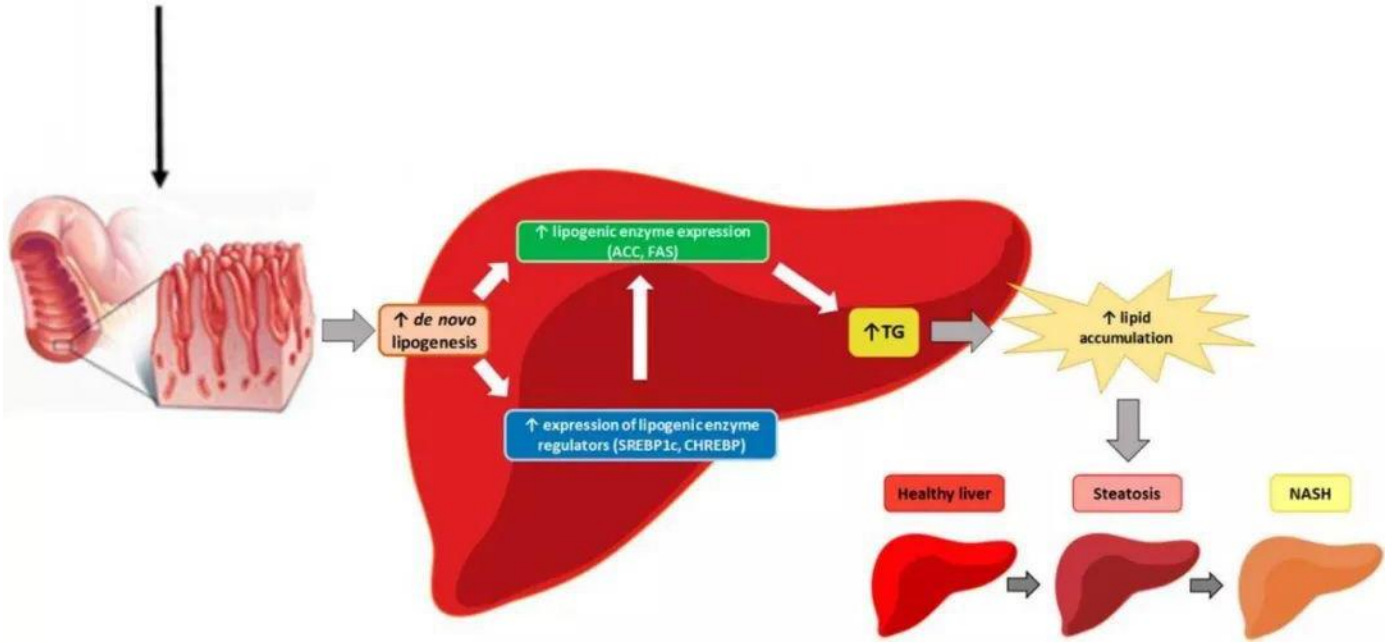
High-sugar food



High-fat food



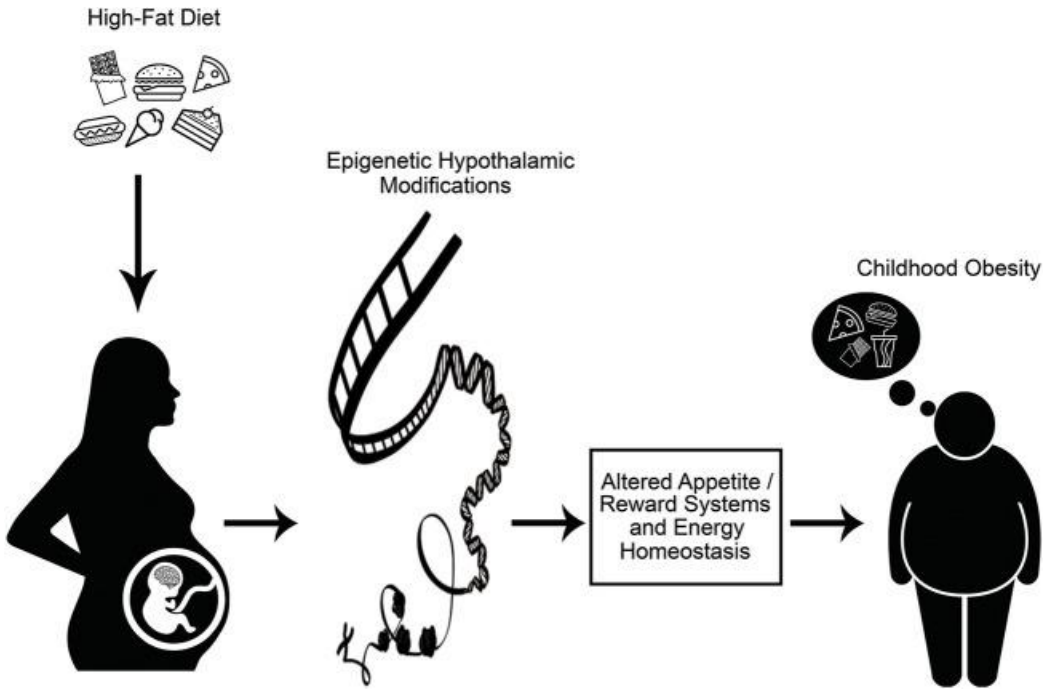
High-salt food



- As the central metabolic organ, the liver becomes the primary target of HFD-induced pathology.
- These lipid deposits progressively develop into fatty liver disease.
- This pathological cascade resembles "chronic hepatic intoxication," characterized by exacerbated oxidative stress, mitochondrial dysfunction, and excessive release of inflammatory cytokines (e.g., TNF-α, IL-6), forming a self-perpetuating vicious cycle.
- During pregnancy, dramatic metabolic adaptations—including estrogen surge and reduced insulin sensitivity—potentially amplify HFD-induced hepatotoxicity.

Introduction

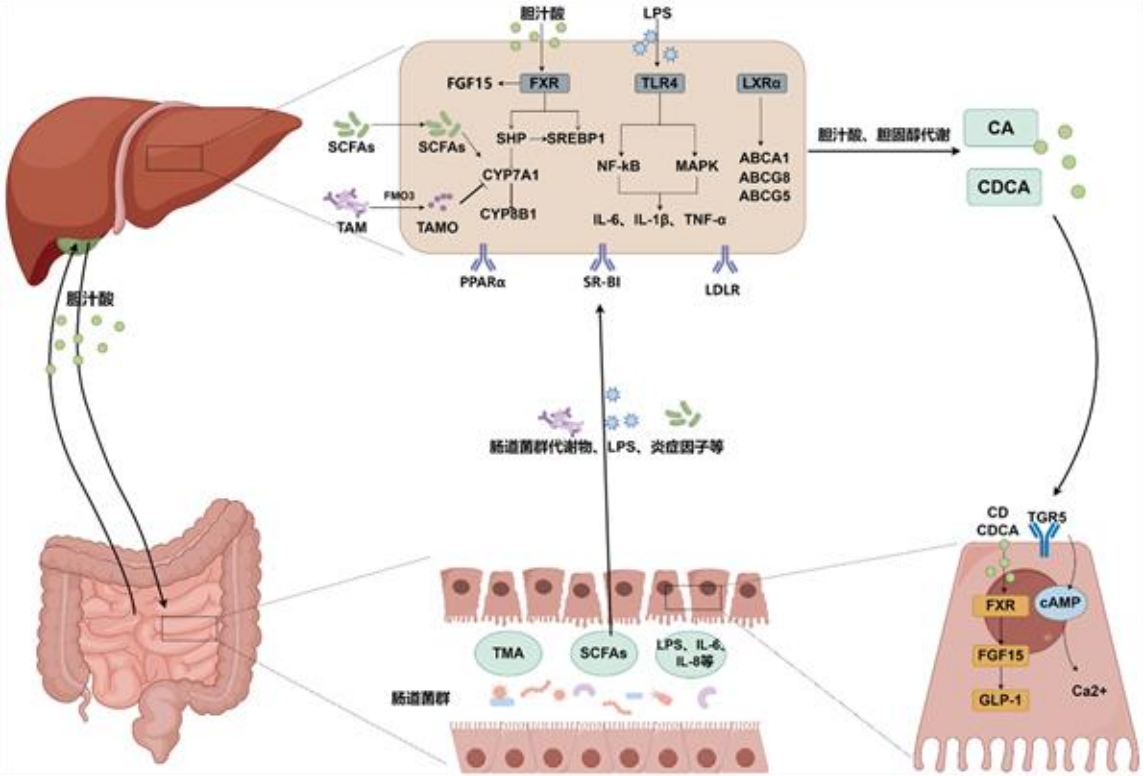
The dual effects of HFD during pregnancy on the mother and offspring



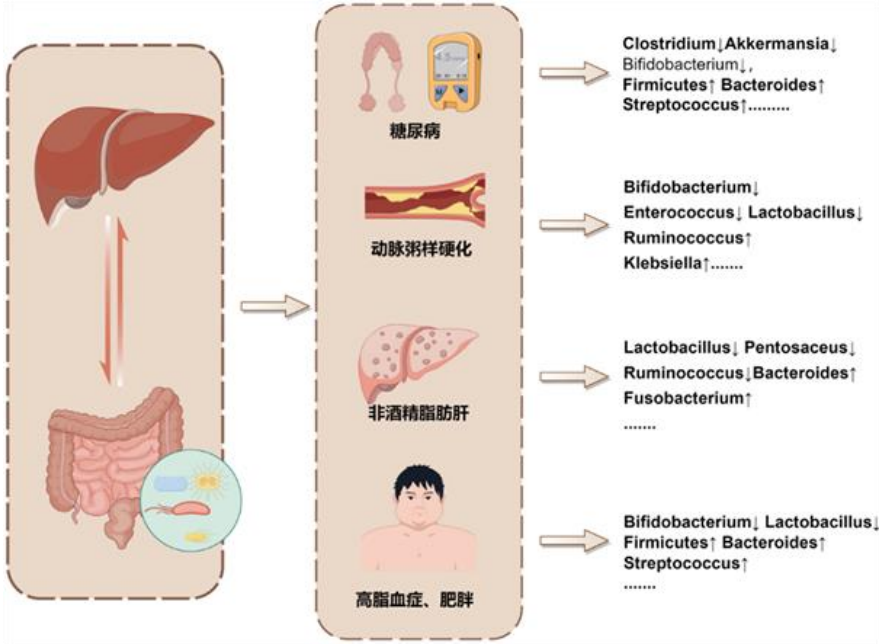
- Epidemiological data indicate that approximately 35% of pregnant women globally exhibit excessive HFD intake, correlating with an 18% incidence of gestational fatty liver disease.
- Maternal metabolic disturbances establish "metabolic memory" in offspring.
- Emerging evidence suggests maternal liver-derived damage-associated molecular patterns (DAMPs) may cross the placental barrier, activating fetal Kupffer cells and initiating chronic hepatic inflammation in offspring.
- This implies a potential triphasic cascade: maternal hepatotoxicity → placental signaling → offspring hepatic programming, though experimental validation is still required.

Introduction

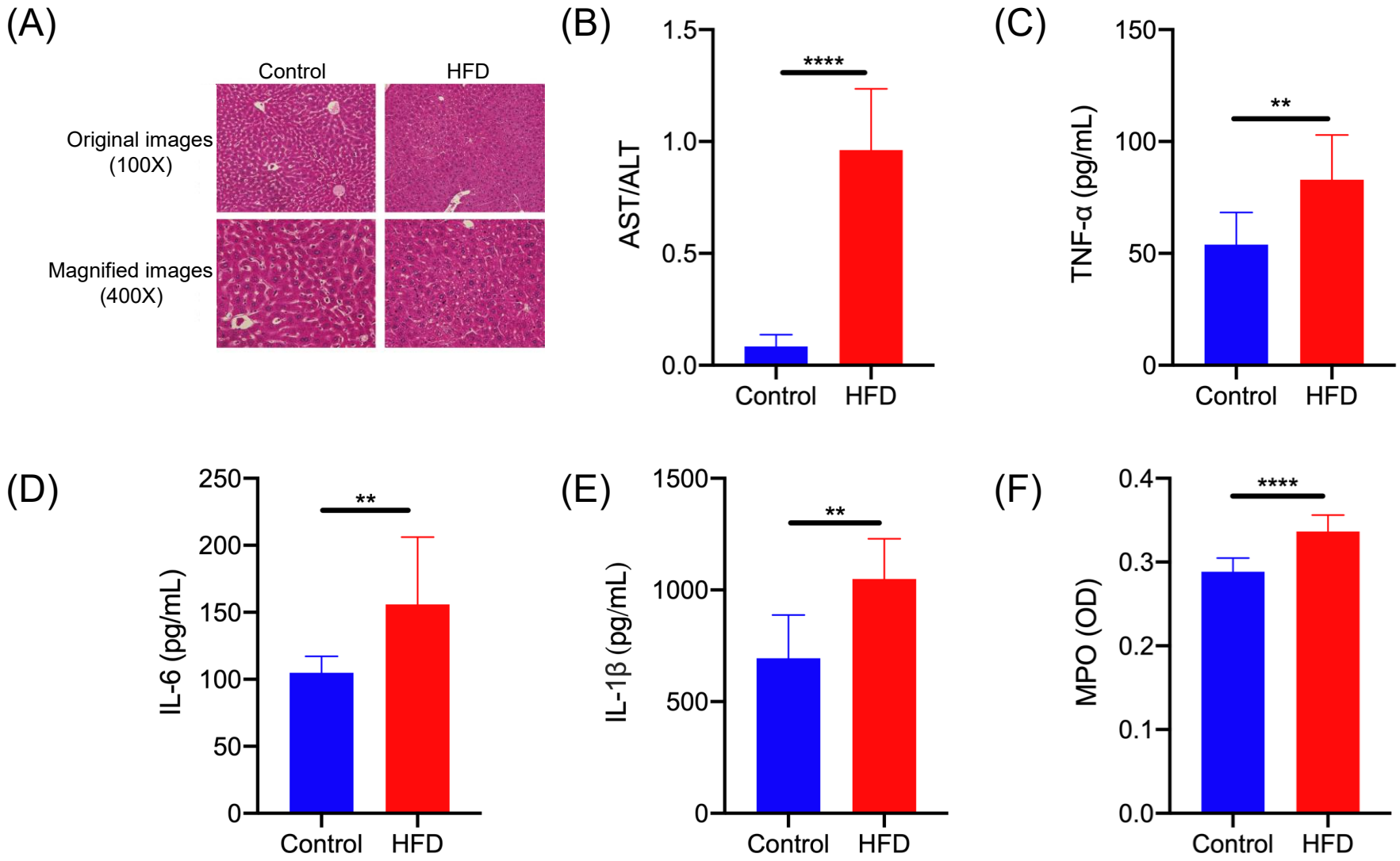
The core role of the gut microbiota in metabolism



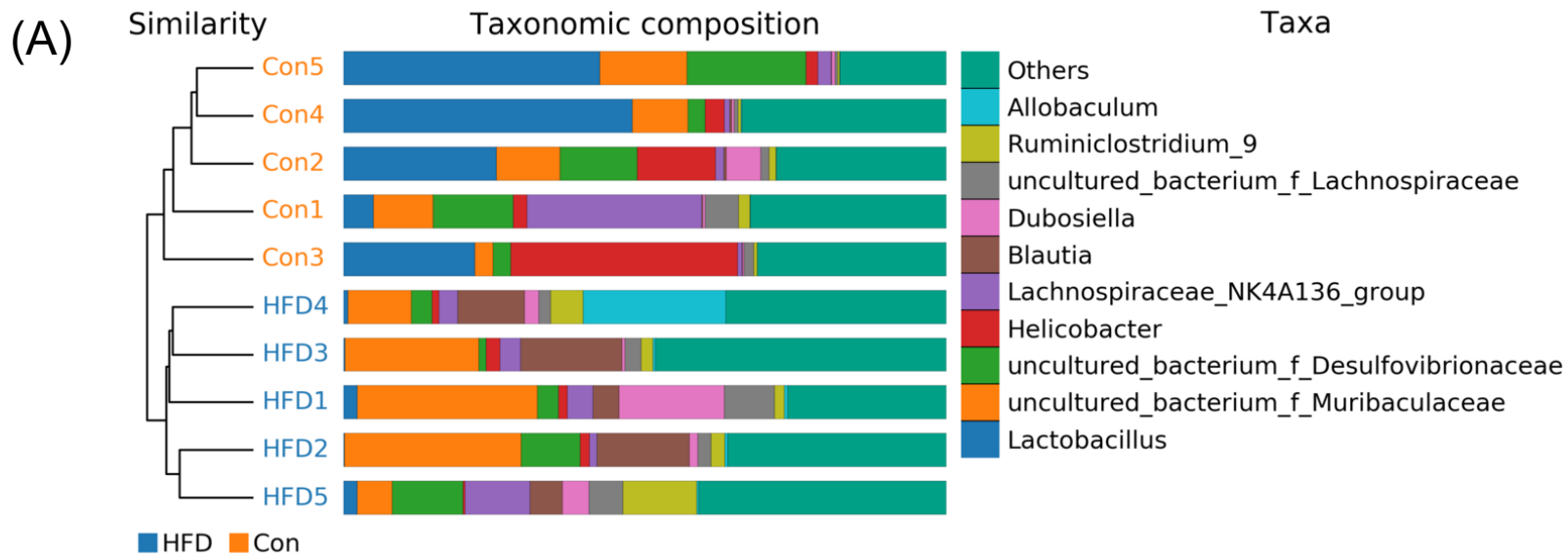
- The gut microbiota, often termed the "hidden organ," demonstrates metabolic capabilities surpassing hepatic function. Through the gut-liver axis, microbial communities engage in intensive molecular crosstalk with the liver.
- Diets exceeding 40% fat content alter bile acid secretion patterns.
- Pregnancy uniquely amplifies microbiota interactions.
- How does gestational HFD modulate gut microbiota to influence maternal hepatic health? Can these microbial alterations transmit hepatic consequences to offspring?

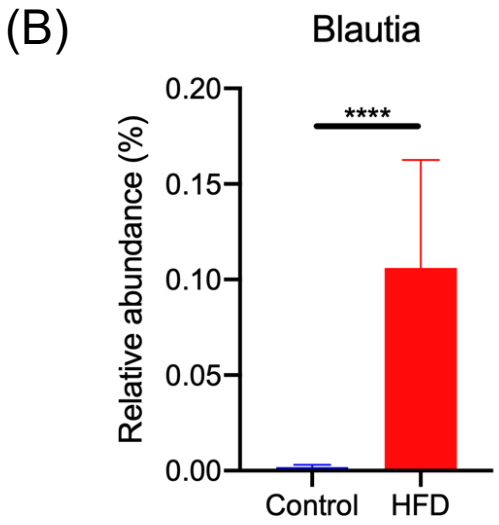


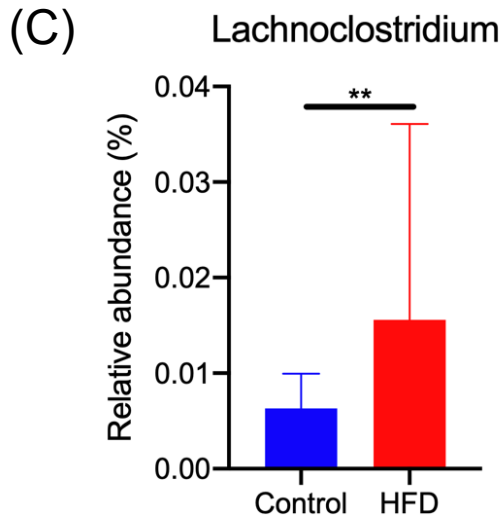
Results

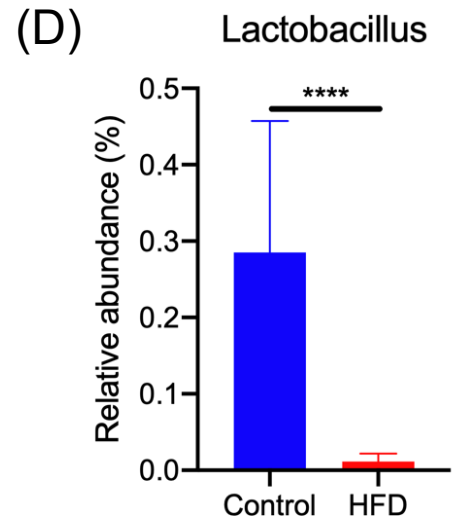

(A)
Control
HFD
Original images (100X)
Magnified images (400X)
(B)
AST/ALT
1.5
1.0
0.5
0.0
****
Control
HFD
(C)
TNF-α (pg/mL)
150
100
50
0
**
Control
HFD
(D)
IL-6 (pg/mL)
250
200
150
100
50
0
**
Control
HFD
(E)
IL-1β (pg/mL)
1500
1000
500
0
**
Control
HFD
(F)
MPO (OD)
0.4
0.3
0.2
0.1
0.0
****
Control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

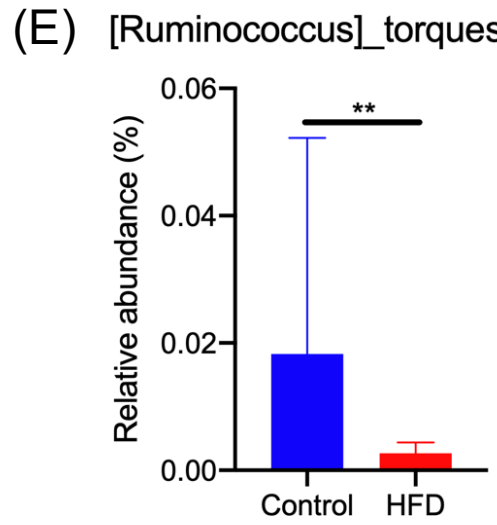
Results


(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

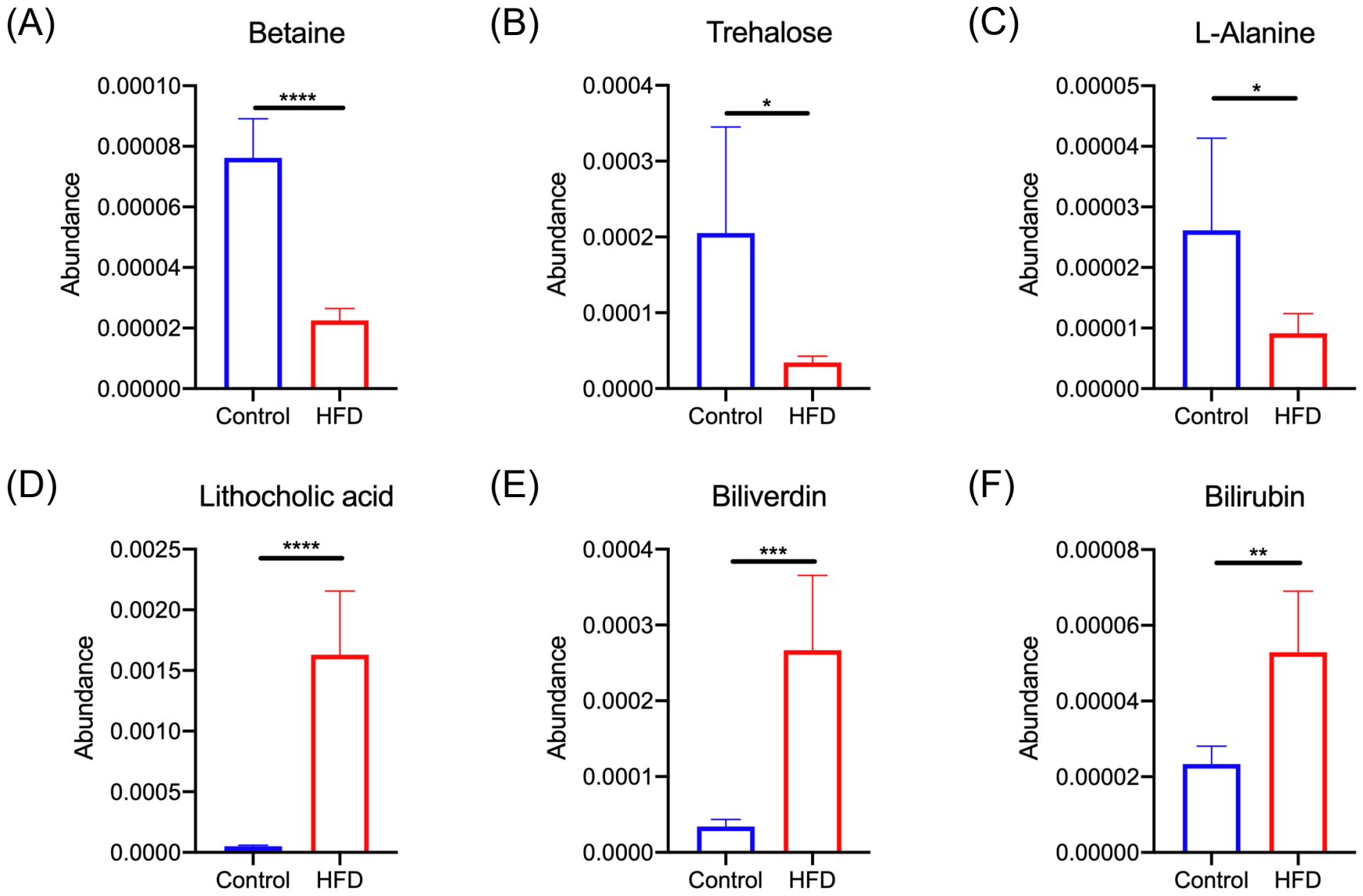

(B)
Blautia
Relative abundance (%)
0.20
0.15
0.10
0.05
0.00
****
Control
HFD


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

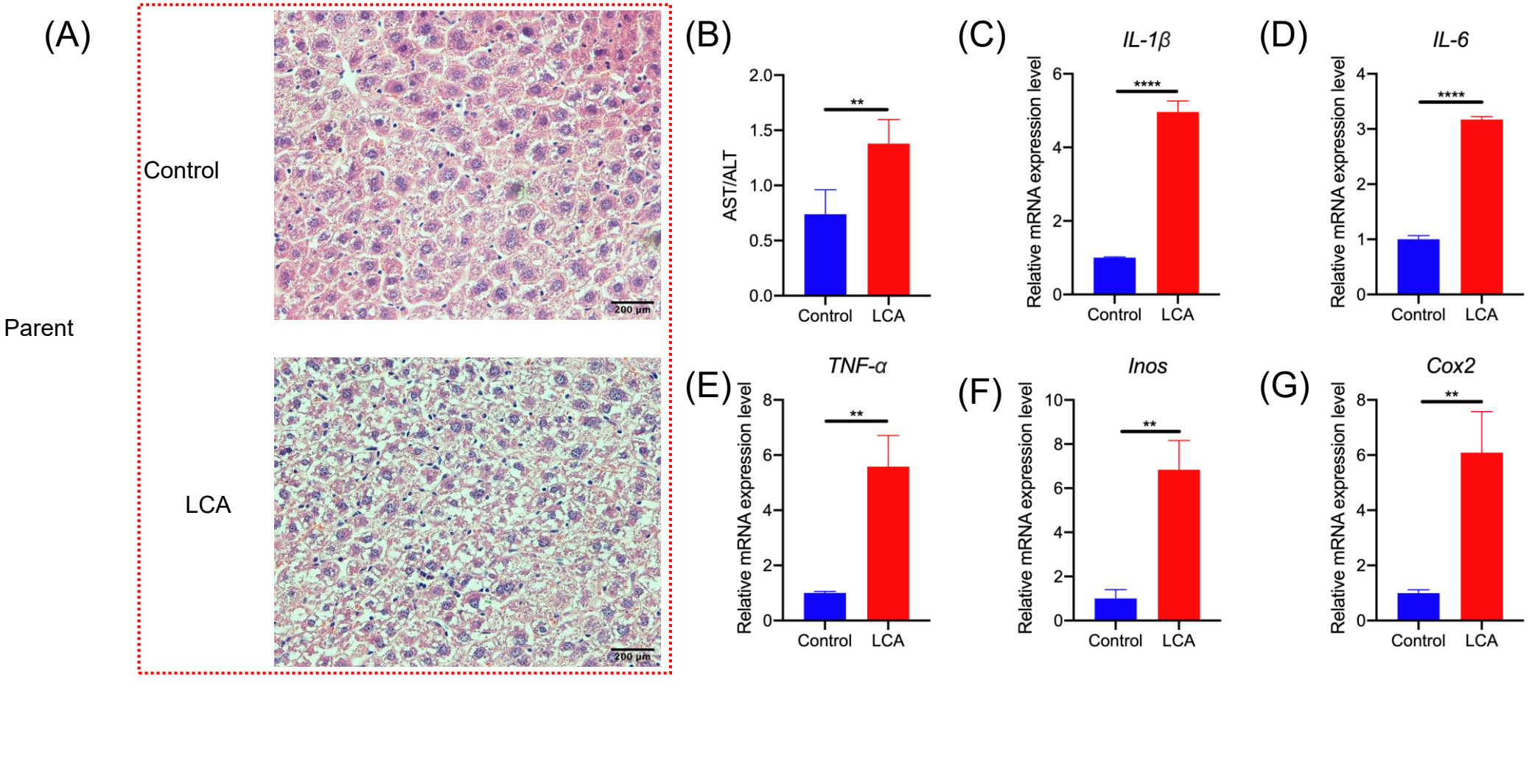

(D)
Lactobacillus
Relative abundance (%)
0.5
0.4
0.3
0.2
0.1
0.0
****
Control
HFD


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

Results


(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

Results


(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

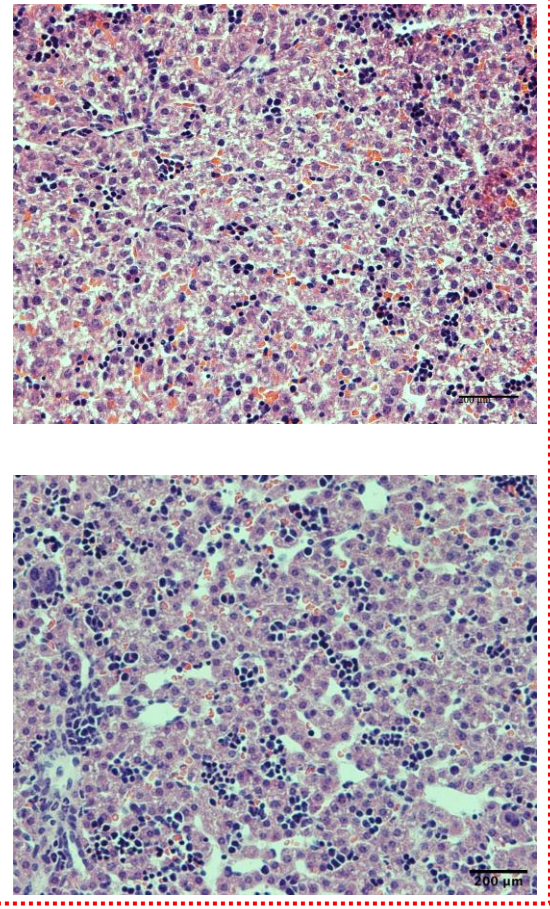
Results

(A)

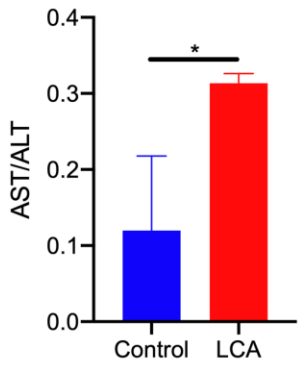
Offspring

Control

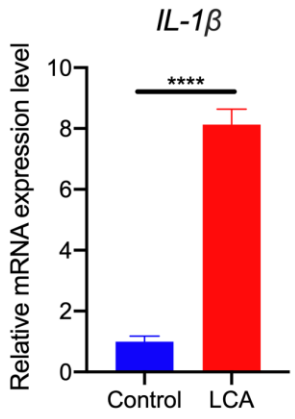
LCA



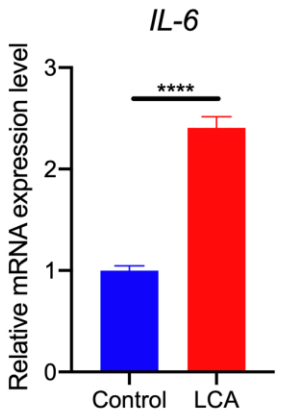
(B)



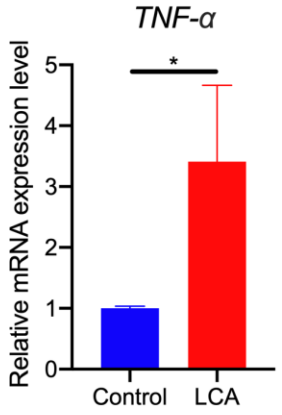
(C)



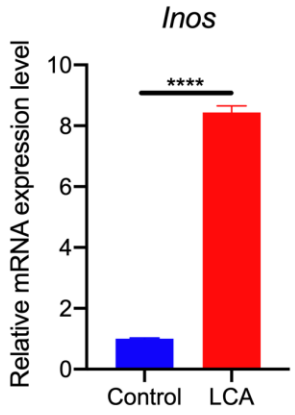
(D)



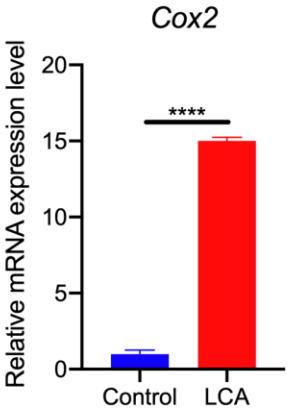
(E)



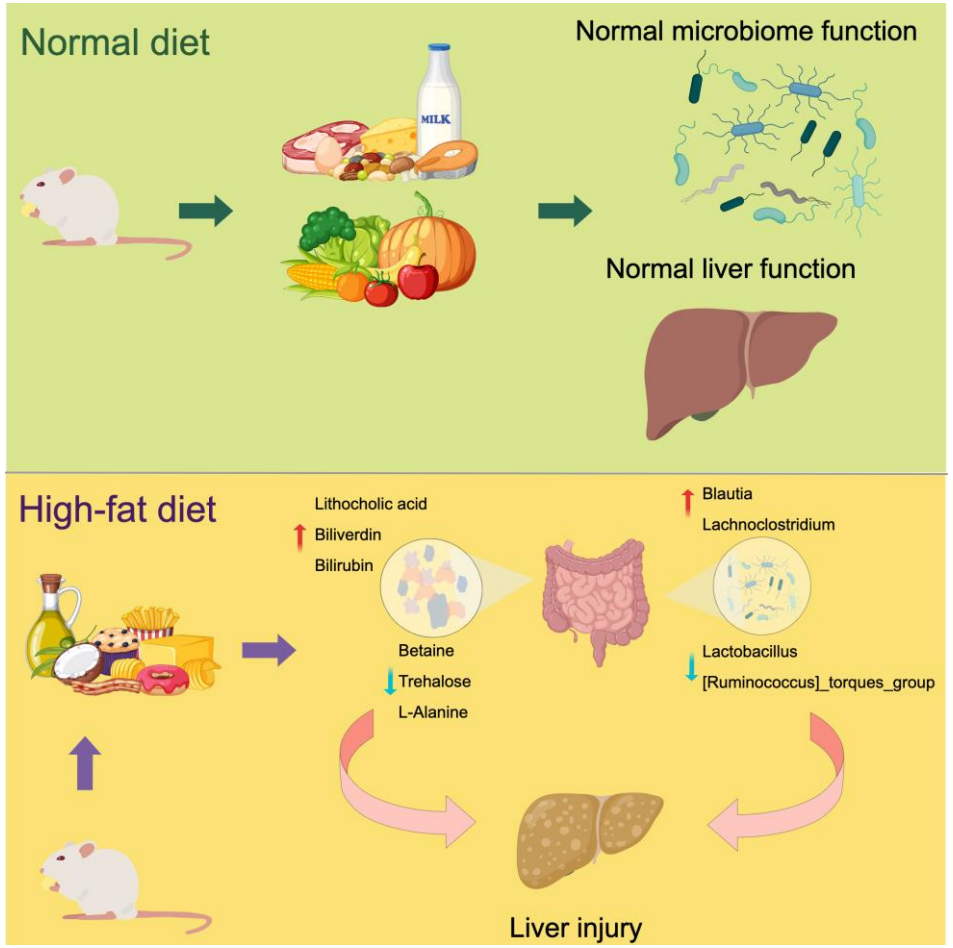
(F)



(G)



Summary

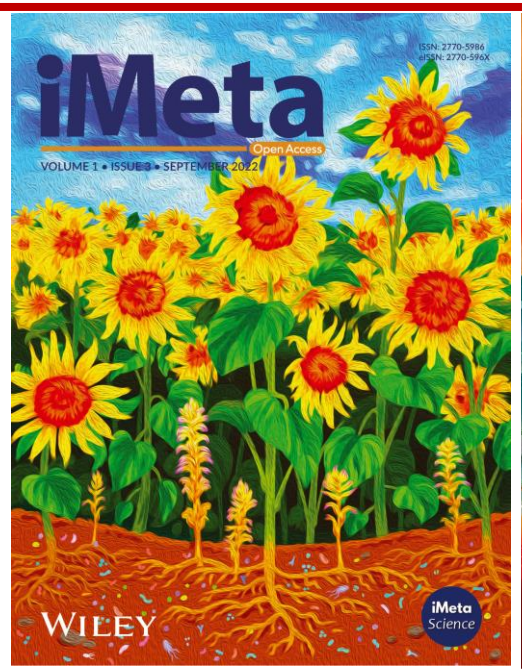


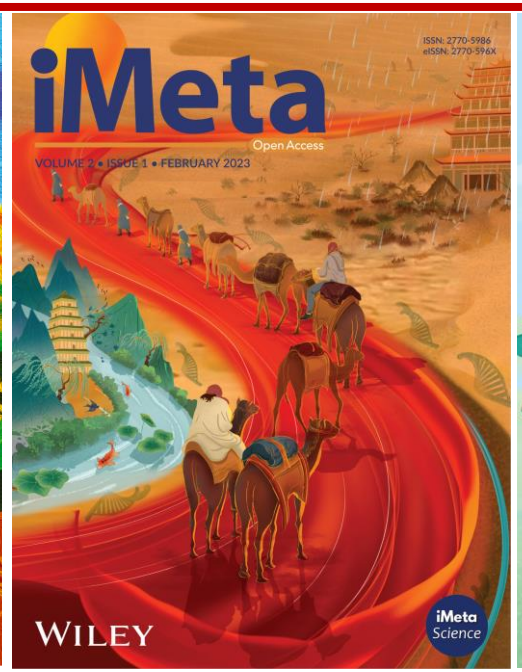
- ❑ High-fat diet during pregnancy induced hepatic steatosis.
- ❑ High-fat diet during pregnancy led to altered gut microbiota and metabolic disruptions.
- ❑ High-fat diet during pregnancy disrupted the intestinal metabolites such as lithocholic acid (LCA).
- ❑ LCA altered in high-fat diet induced hepatic inflammation both in pregnant mice and their offspring.

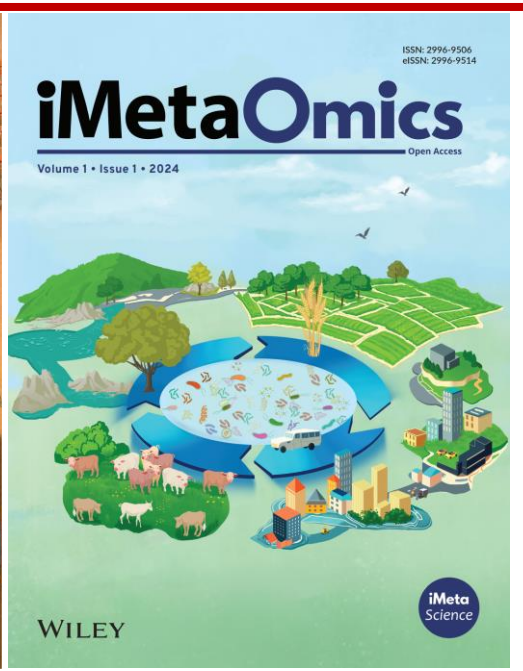
Qian Gong, Yufei Zhang, Juxiong Liu, Shuai Yuan, Huijie Hu, Yu Cao, Shoupeng Fu, et al. 2025. ".The Impact of a High-Fat Diet on Liver Health in Pregnant Mice and Their Offspring: The Role of the Gut-Liver Axis". ***iMetaOmics*** 3: e70026. https://doi.org/10.1002/imo2.70026

iMeta: Integrated metaomics to understand the biology, med and environment

WILEY







"***iMeta***" launched by iMeta Science Society in 2022, impact factor (IF) **23.8**, ranking top 107/21973 in world and 2/161 in the microbiology. It aims to publish innovative and high-quality papers with broad and diverse audiences. **Its scope is similar to *Cell*, *Nature*, *Science***, *Nature Biotechnology/Methods/Microbiology/Medicine/Food*. Its unique features include video abstract, bilingual publication, and social media with 600,000 followers. Indexed by **SCIE/ESI**, **PubMed**, **Google Scholar** etc.

"***iMetaOmics***" launched in 2024, with a **target IF>10, and its scope is similar to *Nature Communications*, *Cell Reports***, *Microbiome, ISME J, Nucleic Acids Research, Briefings in Bioinformatics,* etc.

"***iMetaMed***" launched in 2025, with a **target IF>15, similar to *Med, Cell Reports Medicine***, *eBioMedicine, eClinicalMedicine* etc.

Society: http://www.imeta.science
Publisher: https://wileyonlinelibrary.com/journal/imeta
iMeta: https://wiley.atyponrex.com/journal/IMT2
Submission: iMetaOmics: https://wiley.atyponrex.com/journal/IMO2
iMetaMed: https://wiley.atyponrex.com/journal/IMM3

iMetaScience
iMetaScience

office@imeta.science
imetaomics@imeta.science

Promotion Video

Update 2025/5/21