



中山大学公共卫生学院

SCHOOL OF PUBLIC HEALTH, SUN YAT-SEN UNIVERSITY

Mapping multi-omics predictors of MRI-diagnosed non-alcoholic fatty liver disease in a Chinese prospective cohort

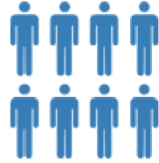
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2024.09.25

Study population and data collection

Discovery (GNHS)

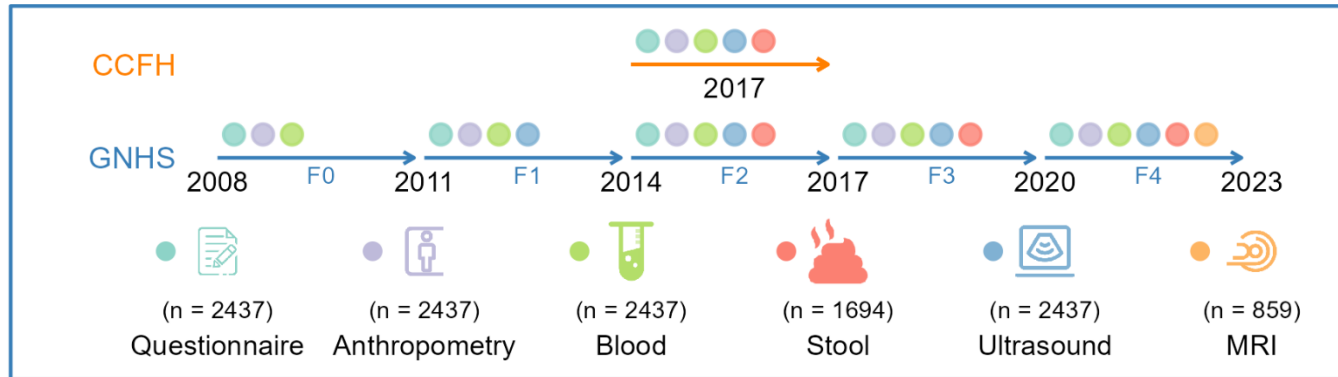


(n = 2437)

Validation (CCFH)



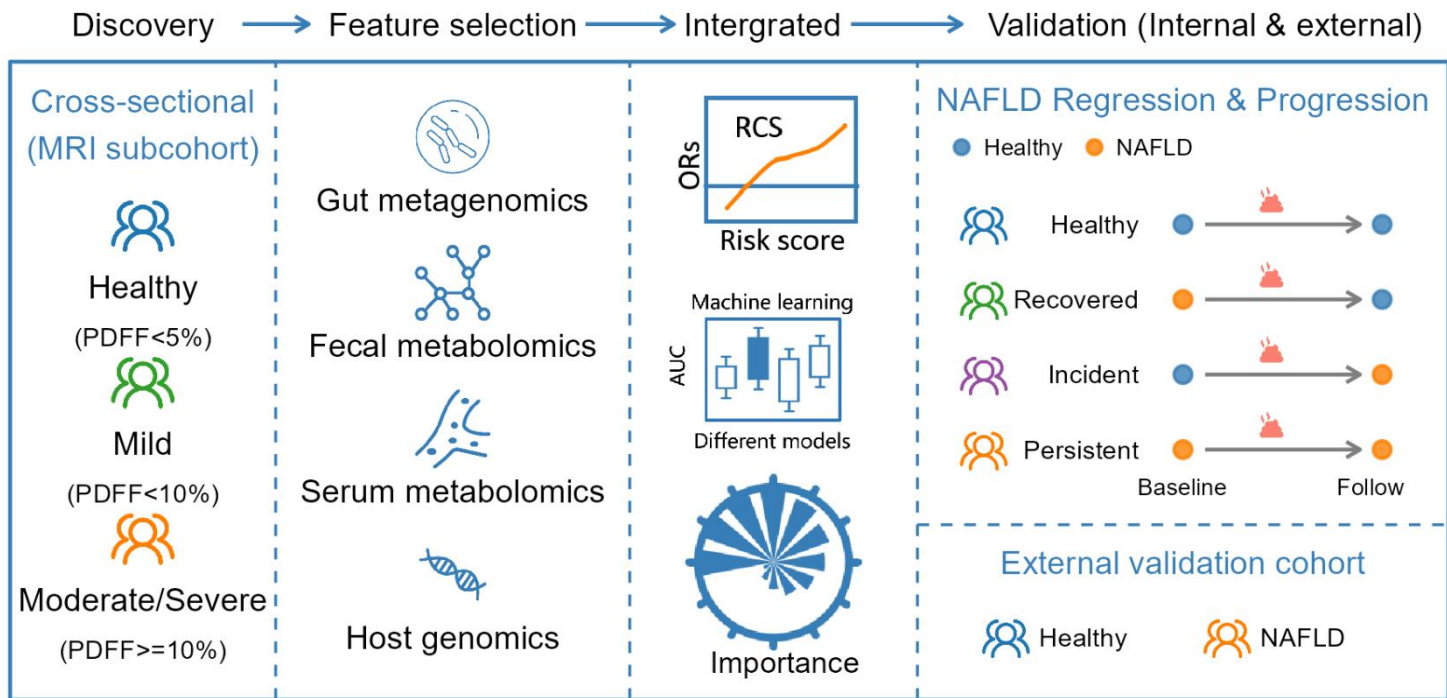
(n = 169)



GNHS: Guangzhou Nutrition and Health Study;

CCFH: Controls of a case-control study of hip fractures.

Study strategy

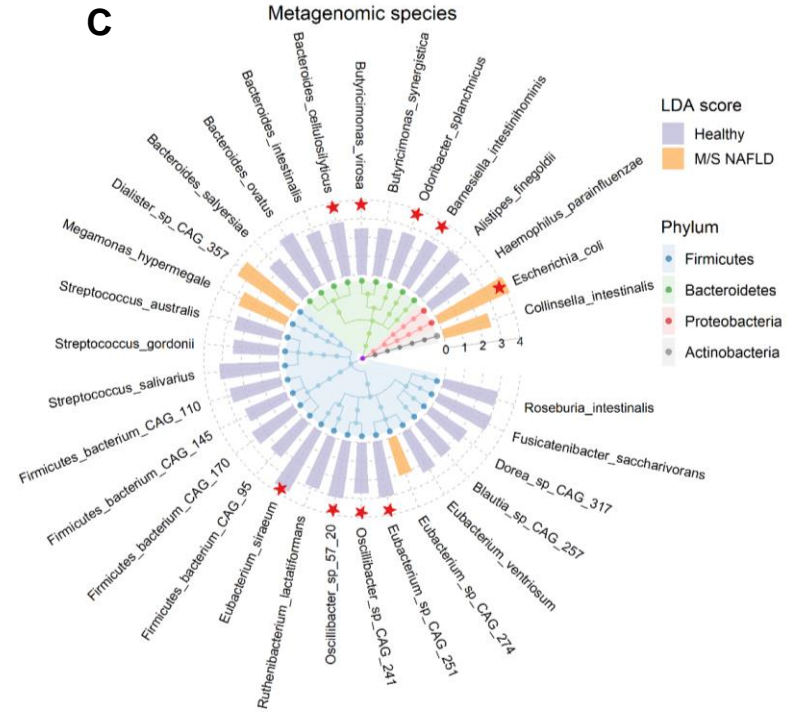
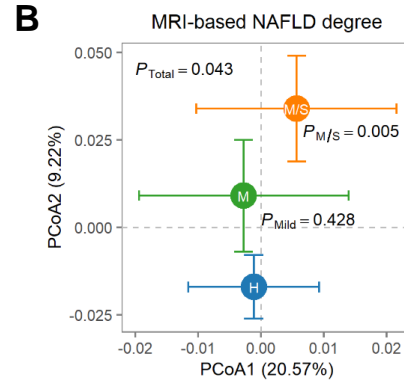
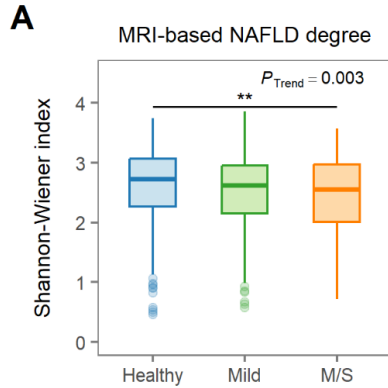


Shotgun metagenomics:

Targeted fecal and serum metabolomics: about 200 metabolites;

Illumina ASA-750K arrays: ≥ 5.7 million single nucleotide polymorphisms

Part1. Gut microbiome and NAFLD



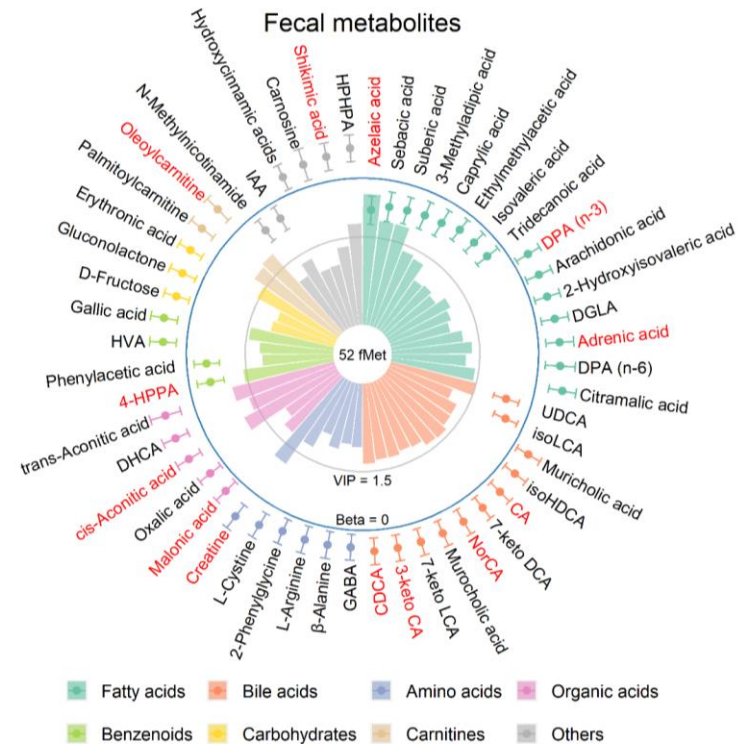
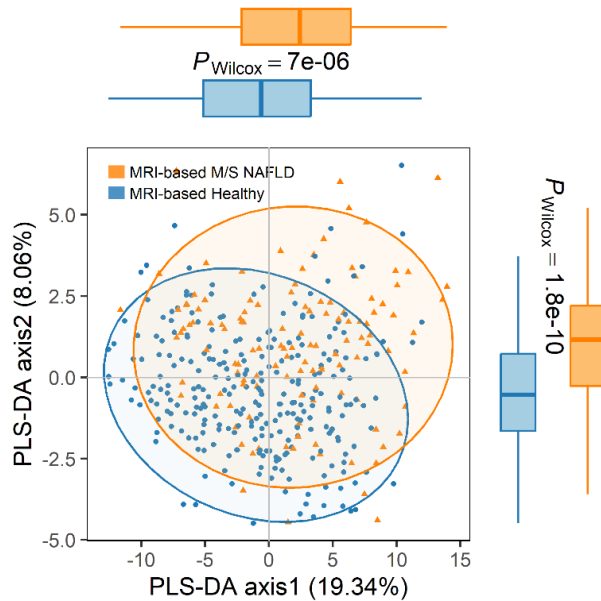
Logistic regression models confirmed 9 species:

alcohol-producing bacteria (e.g., *Escherichia coli*)

SCFA-producing (e.g., *Odoribacter splanchnicus*, and *Bacteroides cellulosilyticus*)

branched-chain amino acids (BCAA)-degrading bacteria (e.g., *Eubacterium siraeum*)

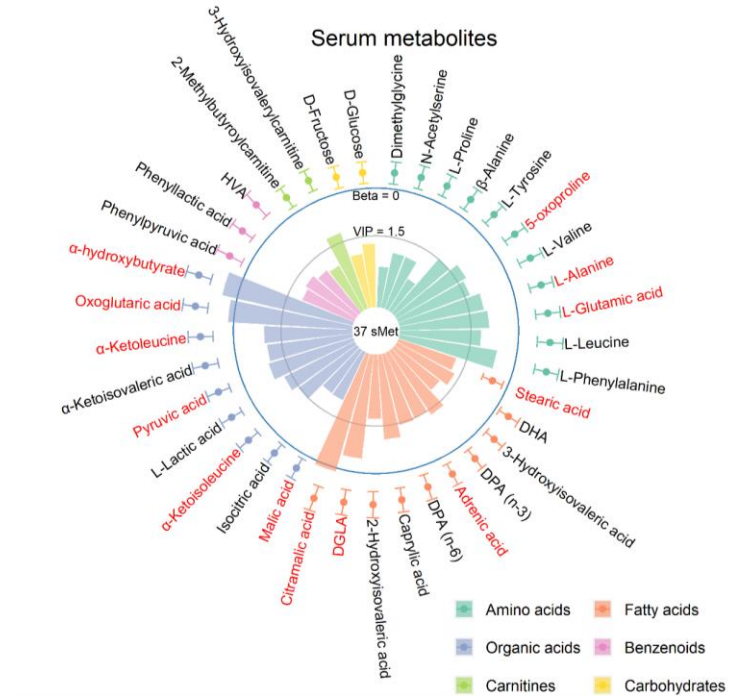
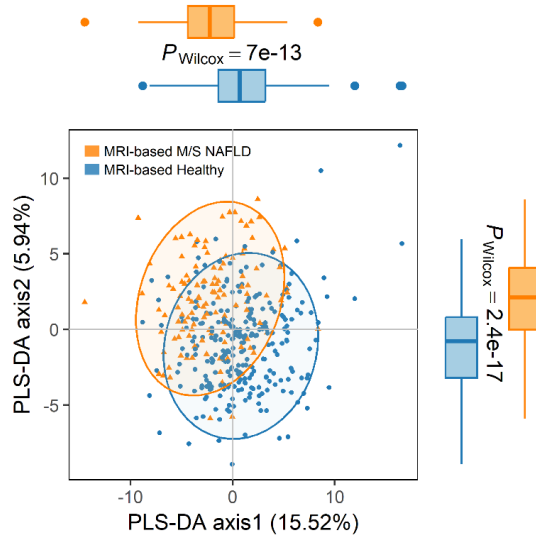
Part1. Fecal metabolites and NAFLD



Top ten important fecal metabolites included:

- Medium-chain dicarboxylic acids (i.e., suberic acid, azelaic acid, and sebacic acid)
- Long-chain acylcarnitine (i.e., oleoylecarnitine and palmitoylecarnitine)

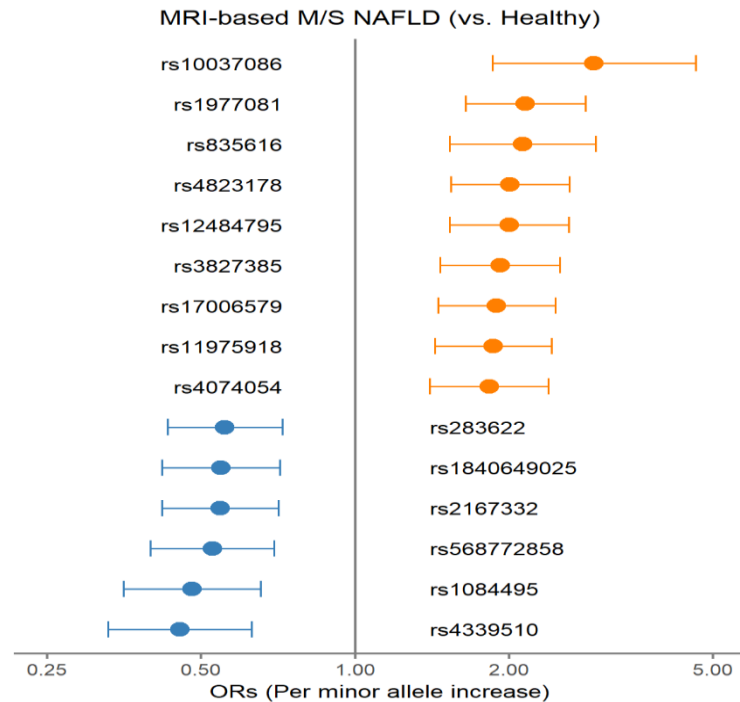
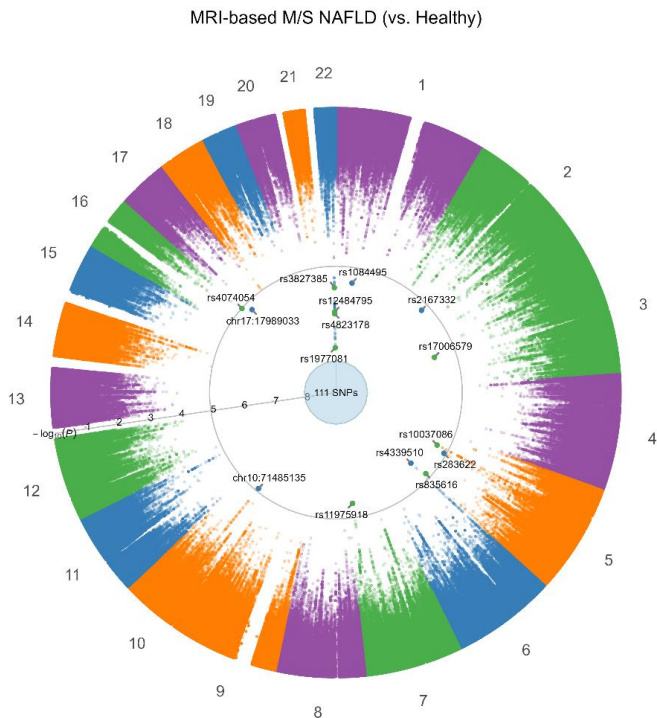
Part1. Serum metabolites and NAFLD



Top ten important serum metabolites mainly included:

α -hydroxybutyrate, and keto acids, such as oxoglutaric acid, pyruvic acid and branched-chain keto acids (BCKAs; ketoleucine and ketoisovaleric acid)

Part1. Host genetics and NAFLD

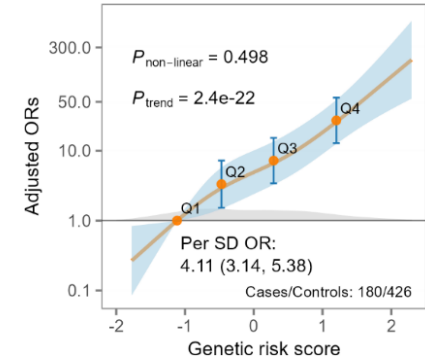
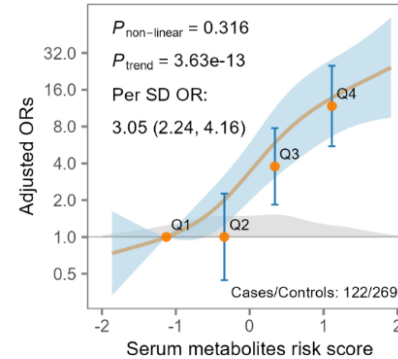
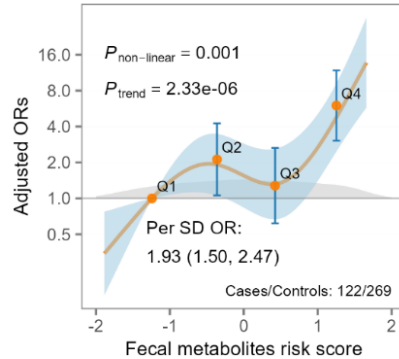
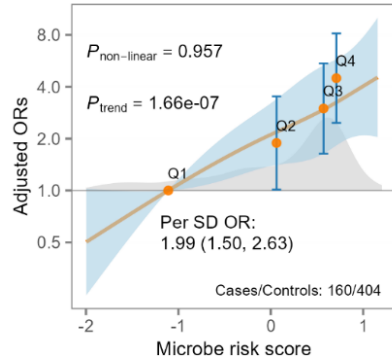


We identified 13 potential genetic loci (e.g., located at *PNPLA3*, *SAMM50*, and *PARVB*) for MRI-based M/S NAFLD

Part2. Omics-based risk scores and NAFLD (Discovery)

A

MRI-based moderate/severe NAFLD (vs. Healthy)



- ✓ Microbe risk scores: 9 species
- ✓ Fecal metabolites risk scores: 13 fecal metabolites
- ✓ Serum metabolites risk scores: 13 serum metabolites
- ✓ Genetic risk scores: 15 genetic variants

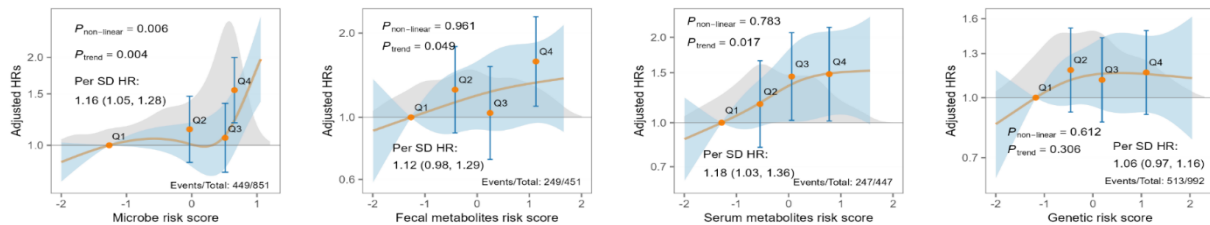
OR(95%CI) in the Q4 (vs. Q1) :

4.49 (2.47, 8.16) for MRS,
4.84 (2.81, 8.33) for FMRS,
11.8 (5.5, 25.1) for SMRS,
27.1 (12.8, 57.5) for GRS

Part2. Omics-based risk scores and NAFLD (Internal & external validation)

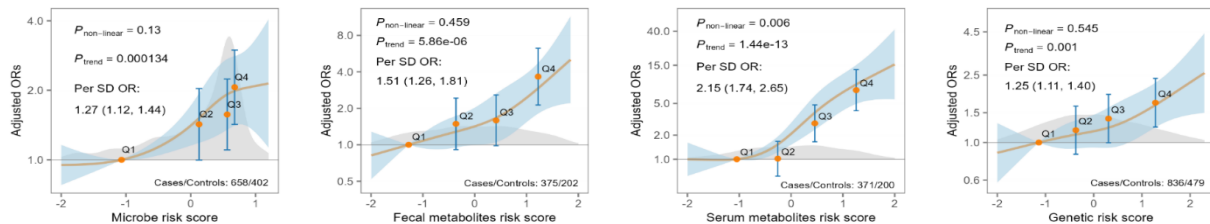
B

US-based incident NAFLD (vs. Healthy)



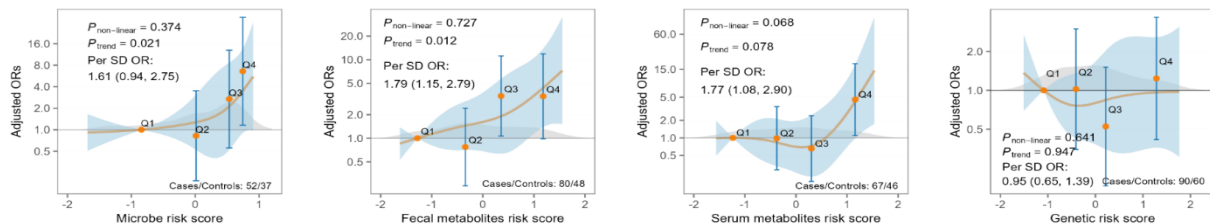
C

US-based persistent NAFLD (vs. Healthy)

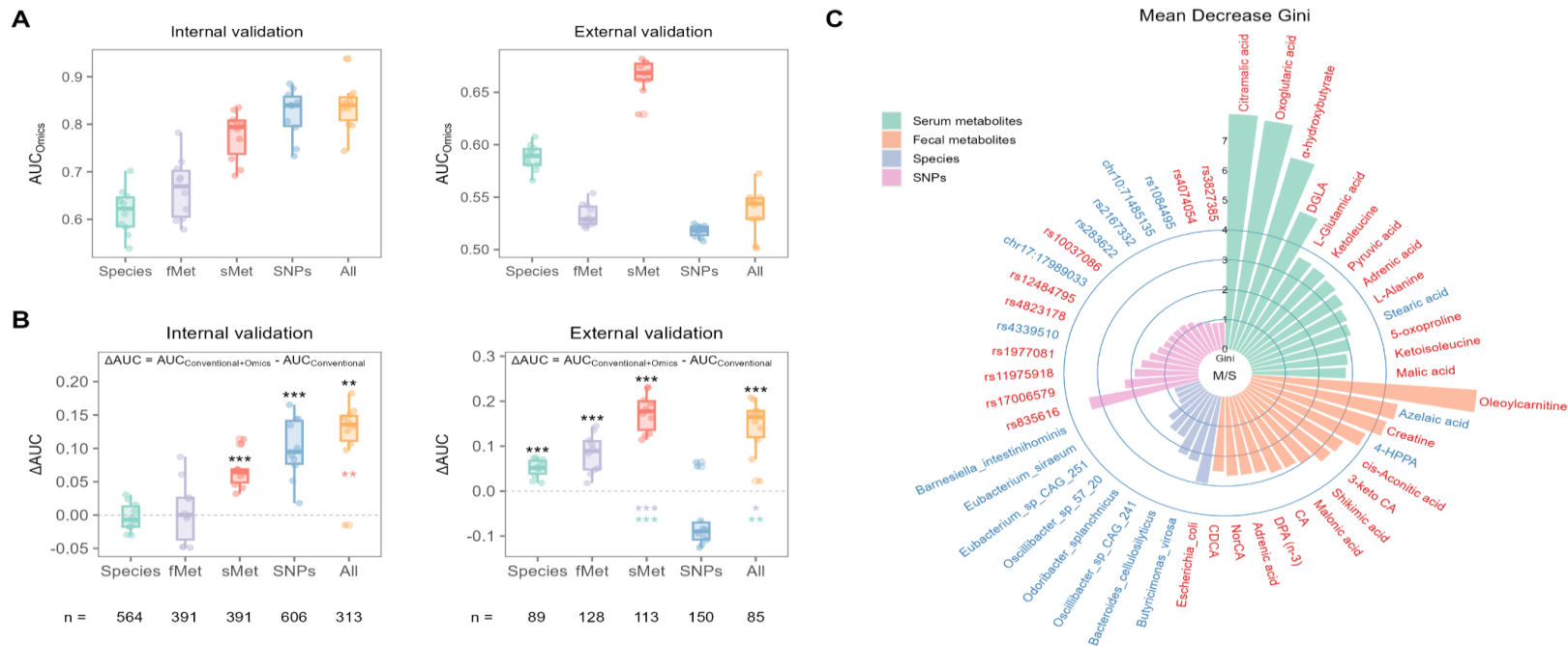


D

US-based NAFLD (External validation)



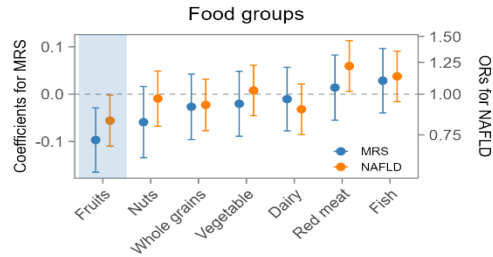
Part3. Predictive capacity and importance of different omics features on NAFLD



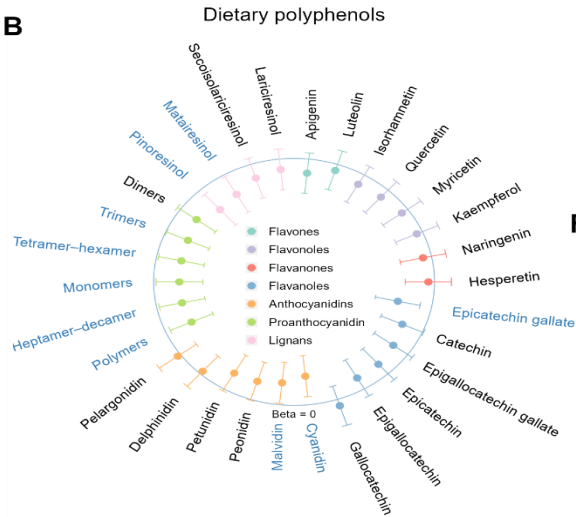
The average AUCs of identified omics features ranged from 0.617 to 0.837 for MRI-based M/S NAFLD in the testing set, and from 0.518 to 0.666 for US-based NAFLD prevalence in the external cohort

Part4. Interplay between dietary factors and gut microbial features for NAFLD

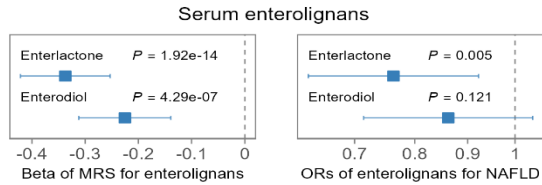
A



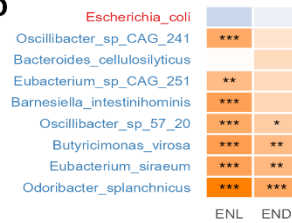
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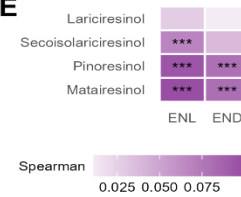
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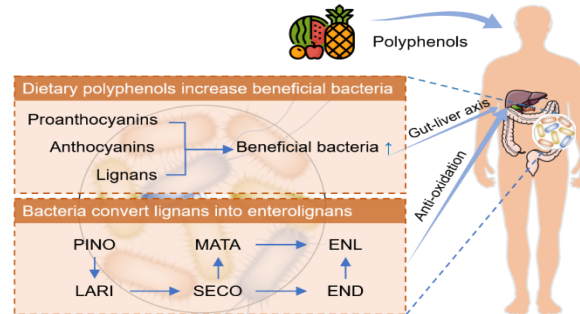
D



E



F



Summary

- Multi-omics predictors for MRI-based moderate/severe NAFLD included:
 - 9 microbial species (e.g., alcohol-producing bacteria),
 - 13 fecal metabolites (e.g., medium-chain dicarboxylic acids),
 - 13 serum metabolites (e.g., α -hydroxybutyrate and keto acids) and
 - 15 genetic variants (e.g., variants in *PNPLA3* and *SAMM50* genes)
- Serum metabolome demonstrated the highest predictive capacity for NAFLD.
- Dietary fruit intake can influence beneficial microbial features, potentially offering protective effects against NAFLD

Acknowledgements

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- Working team

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- Prof. Jusheng Zheng (West Lake University)
- Postgraduates: involved in this study.