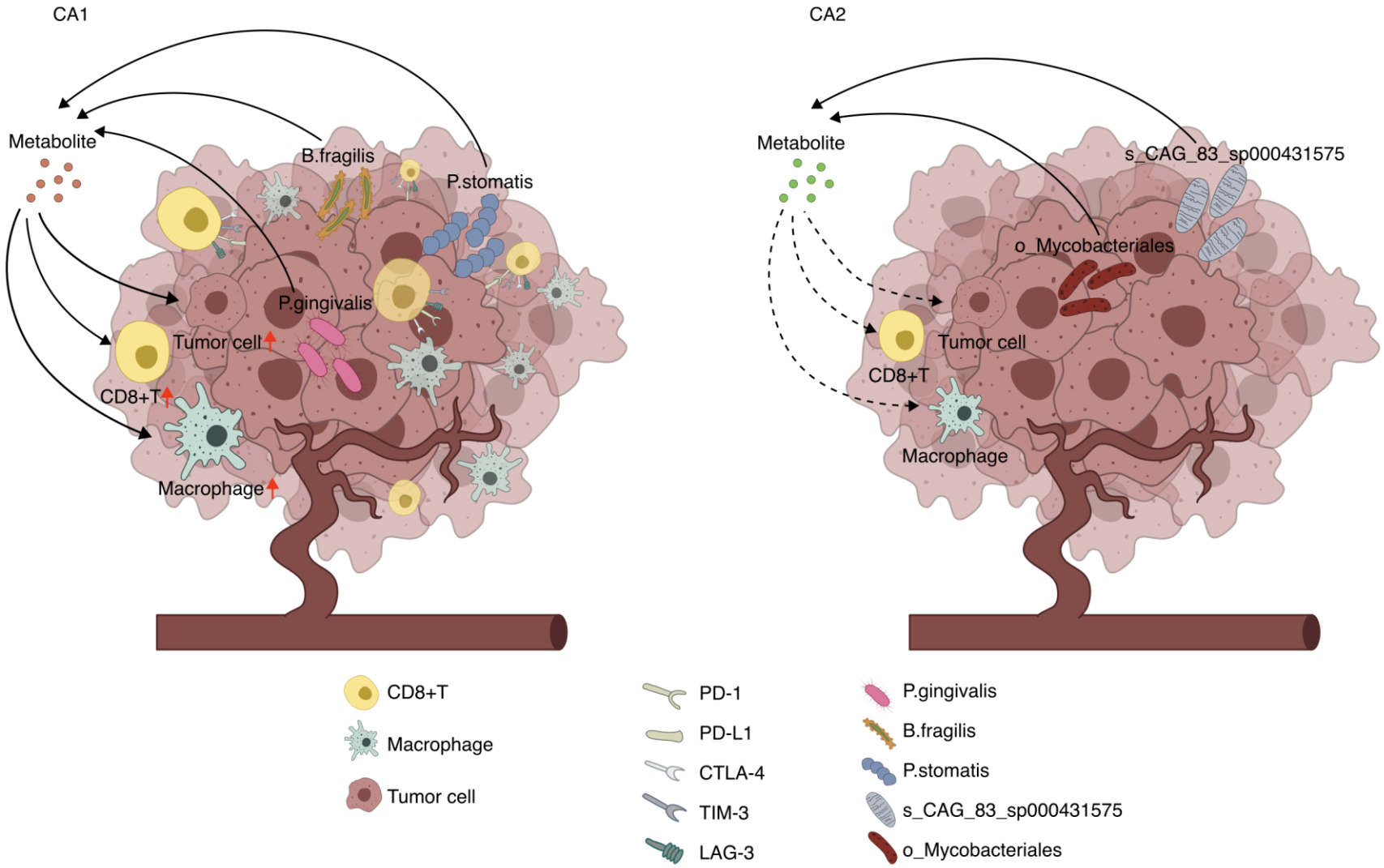
Microbial Influences on Immune Modulation and Colorectal Cancer Progression Through Combined Transcriptomic and Microbiomic Analysis

Shuting Xia[1,2#], Likun Wang[3#], Yangzhuo Xu[3#], Jiaqi Zhang[1#], Zeyang Zhou[4#], Libing Sun[5#], Heng Li[1], Chungen Xing[4], Jialu Mao[4], Yina Liu[1], Fulin Yang[1], Ling Zhong[1], Jiancheng Xu[1,2*], Xiaodong Yang[1,2,4*], Zhemin Zhou[1,2*]

[1]The Second Affiliated Hospital of Soochow University, Cancer Institute, Soochow University
[2]National Center of Technology Innovation for Biopharmaceuticals, Suzhou Biomedical Industry Innovation Center
[3]School of Public Health, Suzhou Medical College, Soochow University
[4]Department of General Surgery, The Second Affiliated Hospital of Soochow University
[5]The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou Municipal Hospital, Gusu School, Nanjing Medical University

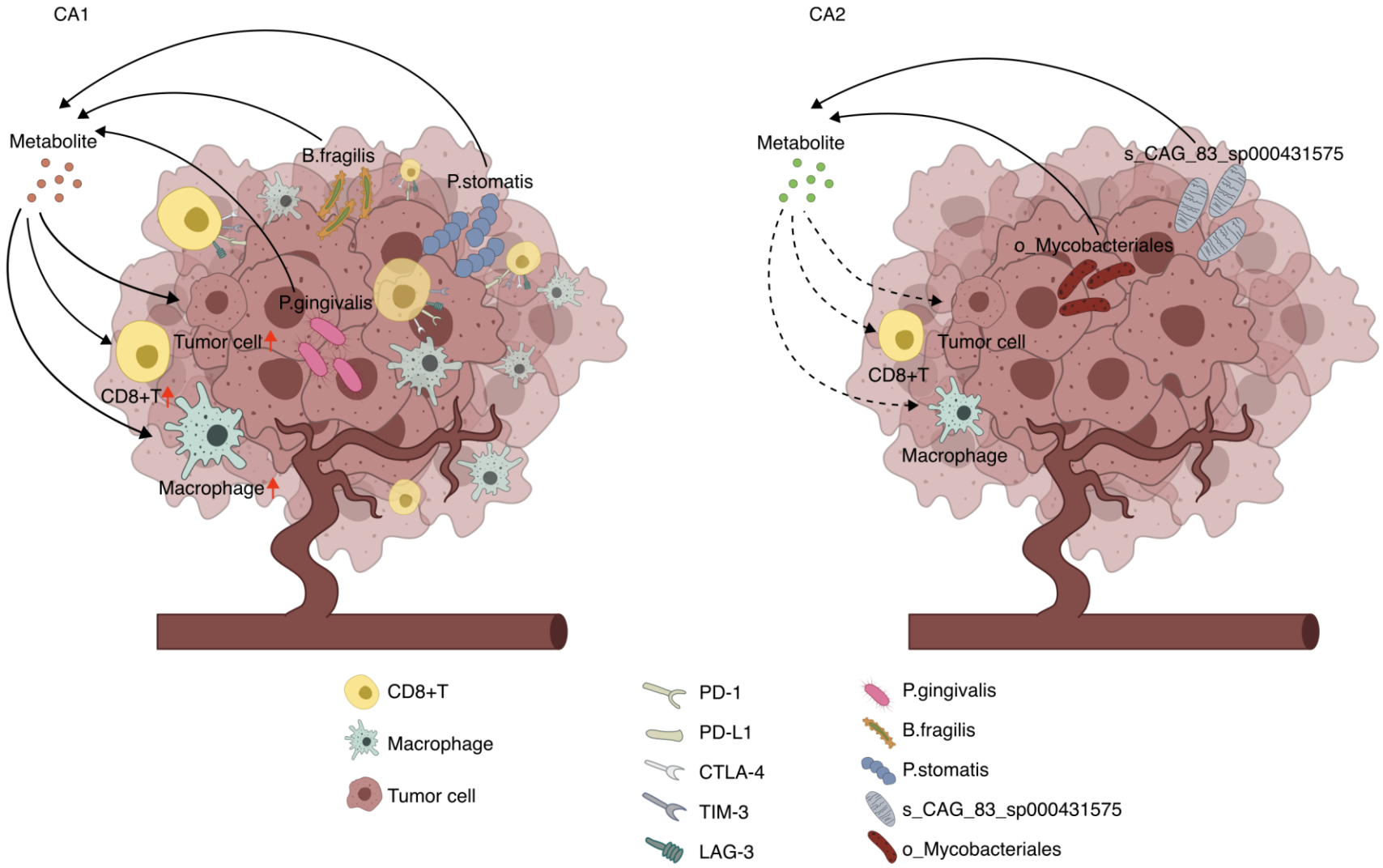
Shuting Xia, Likun Wang, Yangzhuo Xu, Jiaqi Zhang, Zeyang Zhou, Libing Sun, Heng Li, et al. 2025. Microbial Influences on Immune Modulation and Colorectal Cancer Progression Through Combined Transcriptomic and Microbiomic Analysis. ***iMetaOmics*** 2: e70072. https://doi.org/10.1002/imo2.70072

Graphical Abstract



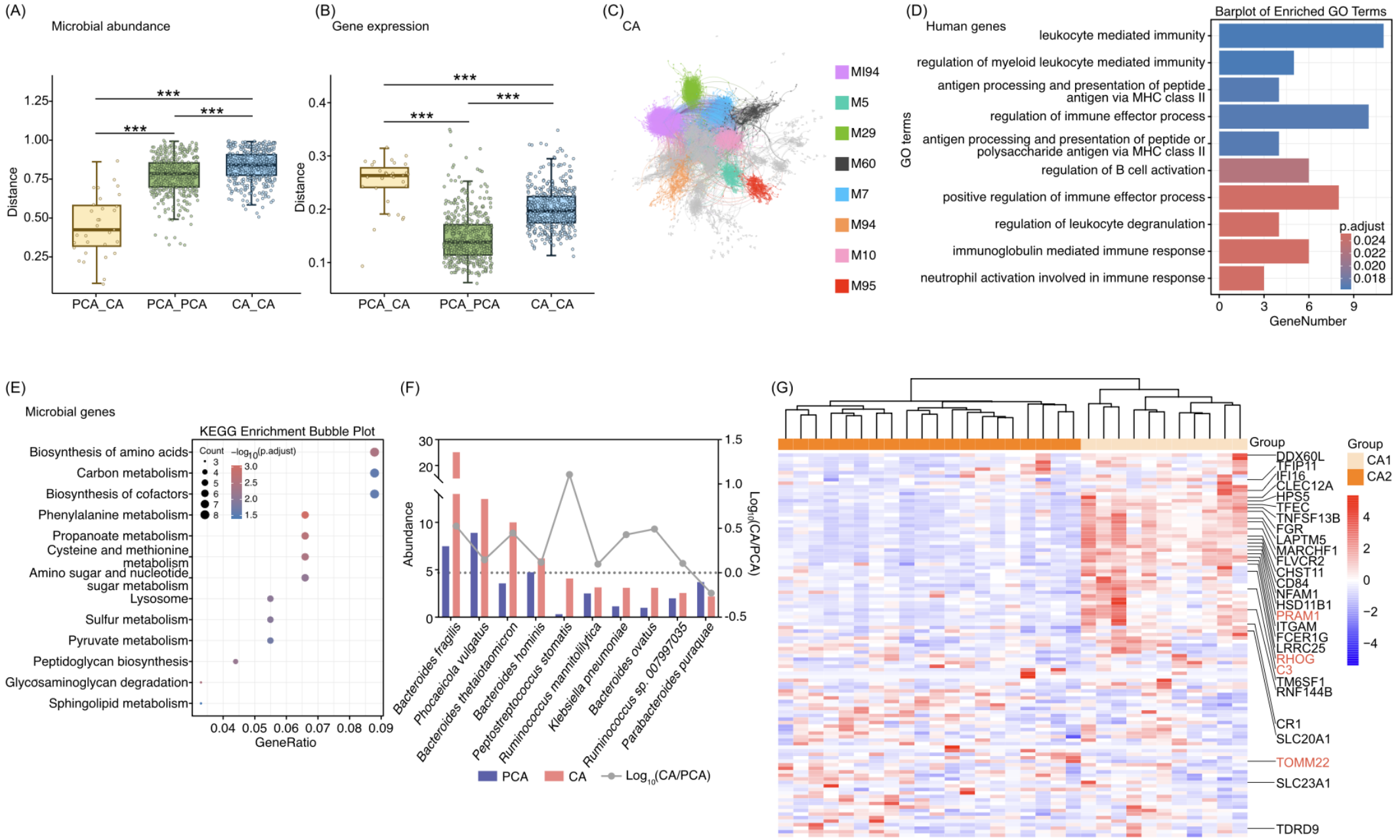
- **Left (CA1 Subtype):** Immune exhaustion, poor prognosis, enriched with pathobionts (*P. gingivalis*, *B. fragilis*), upregulated GABA metabolites.
- **Right (CA2 Subtype):** Immune suppression, better prognosis, enriched with health-associated microbes.

Graphical Abstract

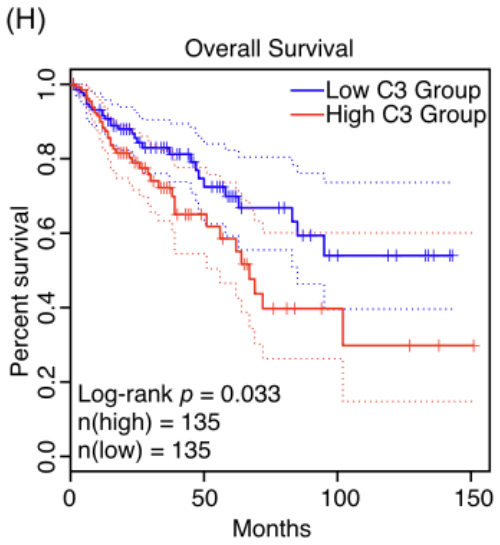


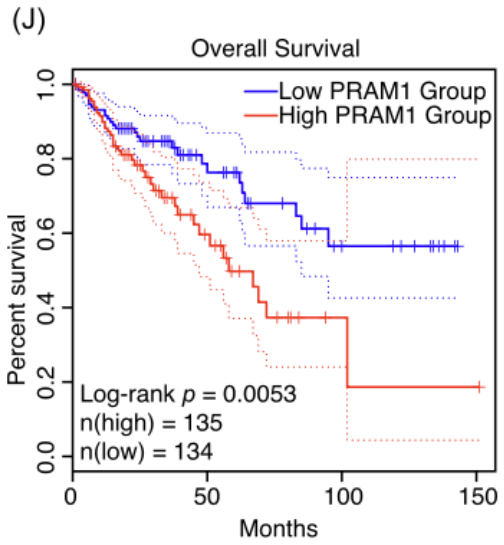
- **Samples:** 31 pairs of colorectal cancer tumor tissues (CA) and adjacent normal tissues (PCA).
- **Technologies:** Transcriptome sequencing (RNA-seq) + In situ microbiome sequencing (2b-RAD-M).
- **Core Method:** Construction of host-microbiome co-expression networks to identify the core immune module (M95).
- **Subtyping:** Tumor samples were classified into CA1 and CA2 subtypes based on the M95 module.

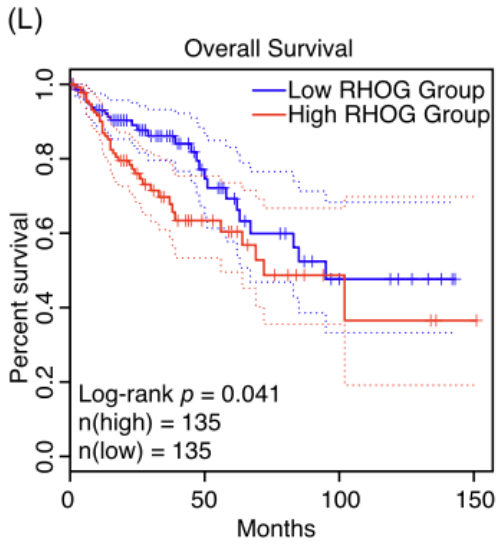
Multi-omics Analysis Strategy

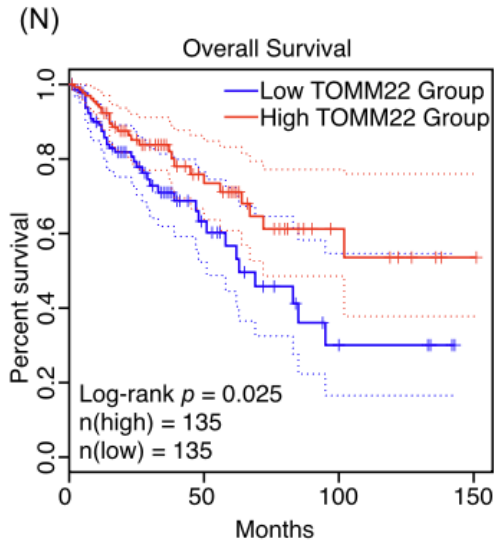


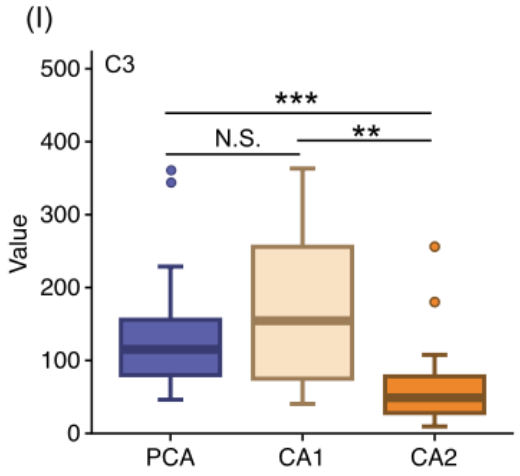
Subtype Features: Immune Exhaustion and Prognosis

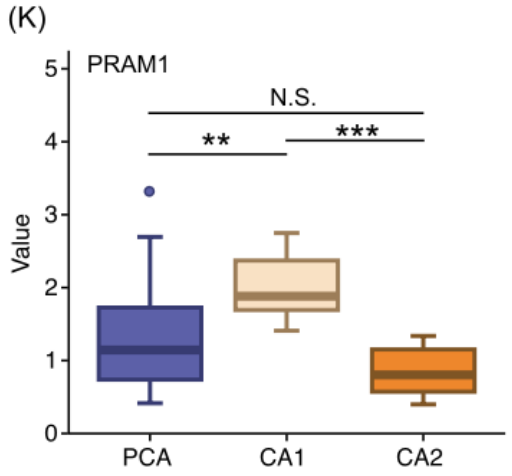


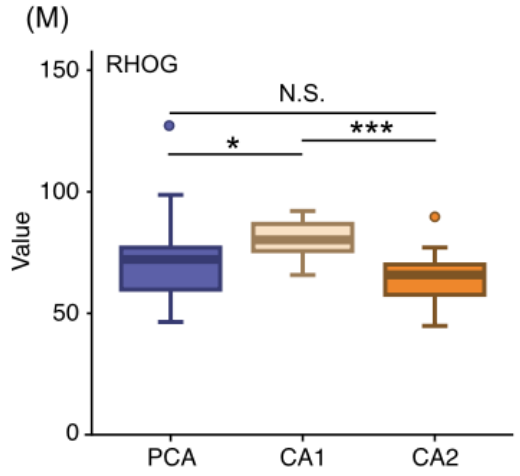


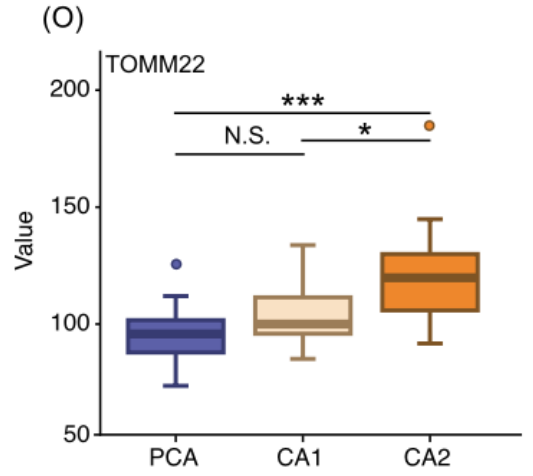






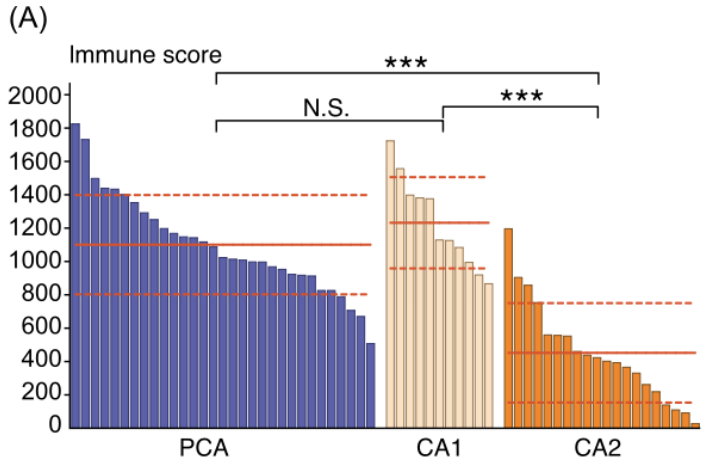


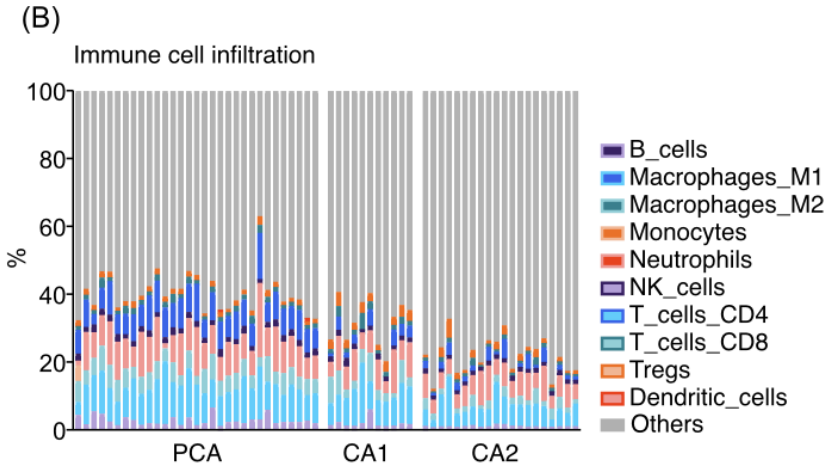


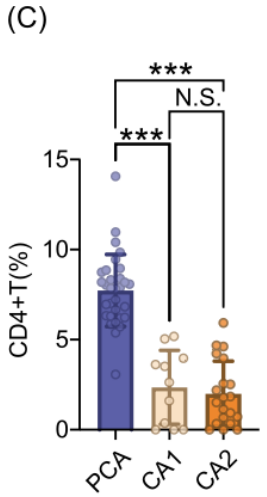


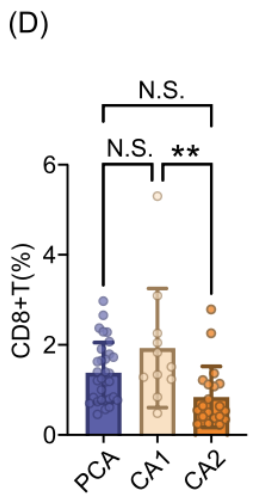
- **Prognosis:** The survival rate of the CA1 subtype is significantly lower than that of CA2.

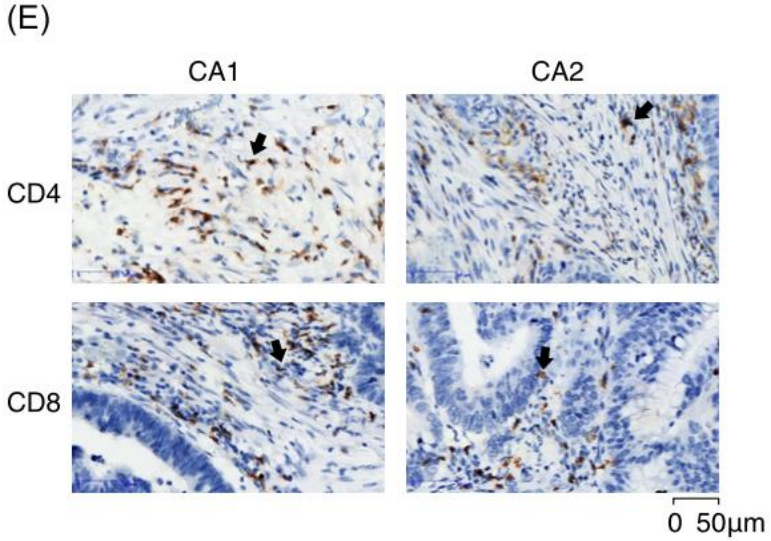
Subtype Features: Immune Exhaustion and Prognosis

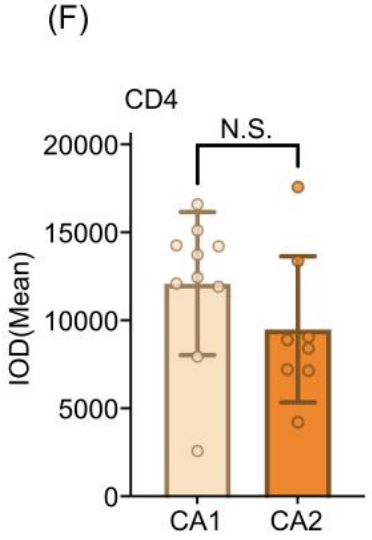


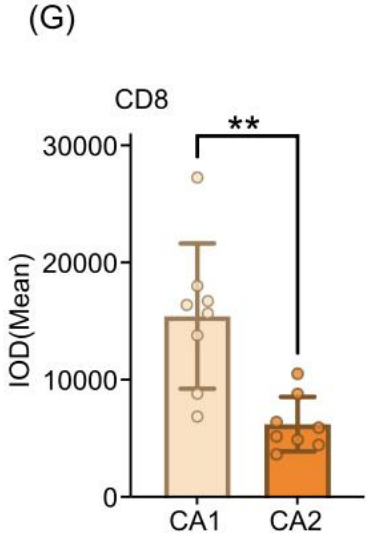


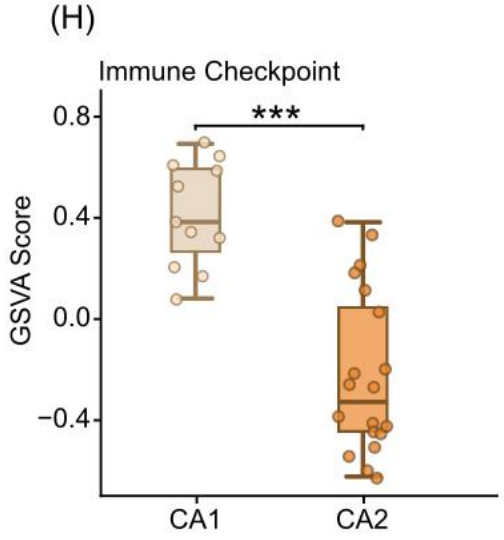






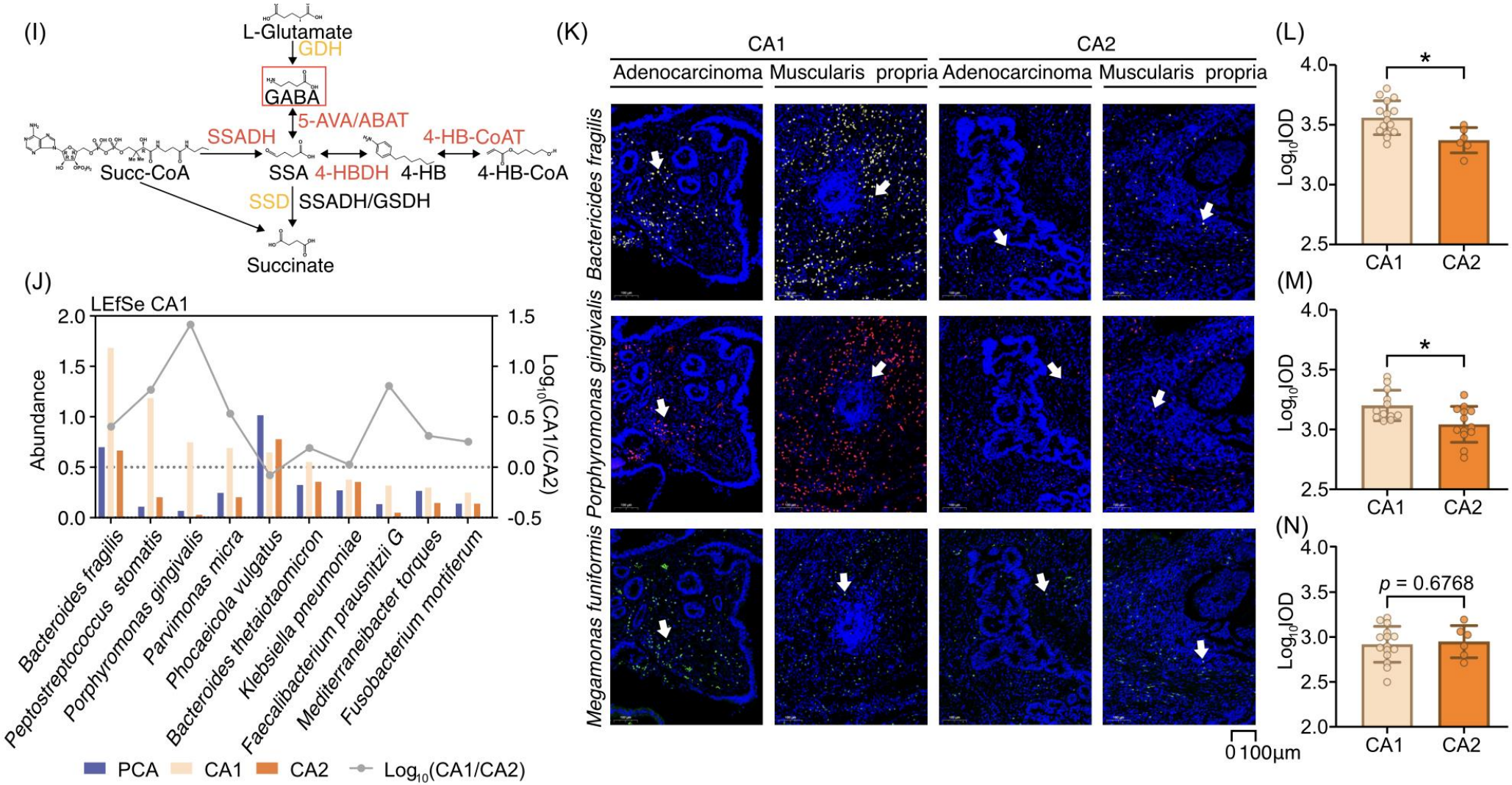






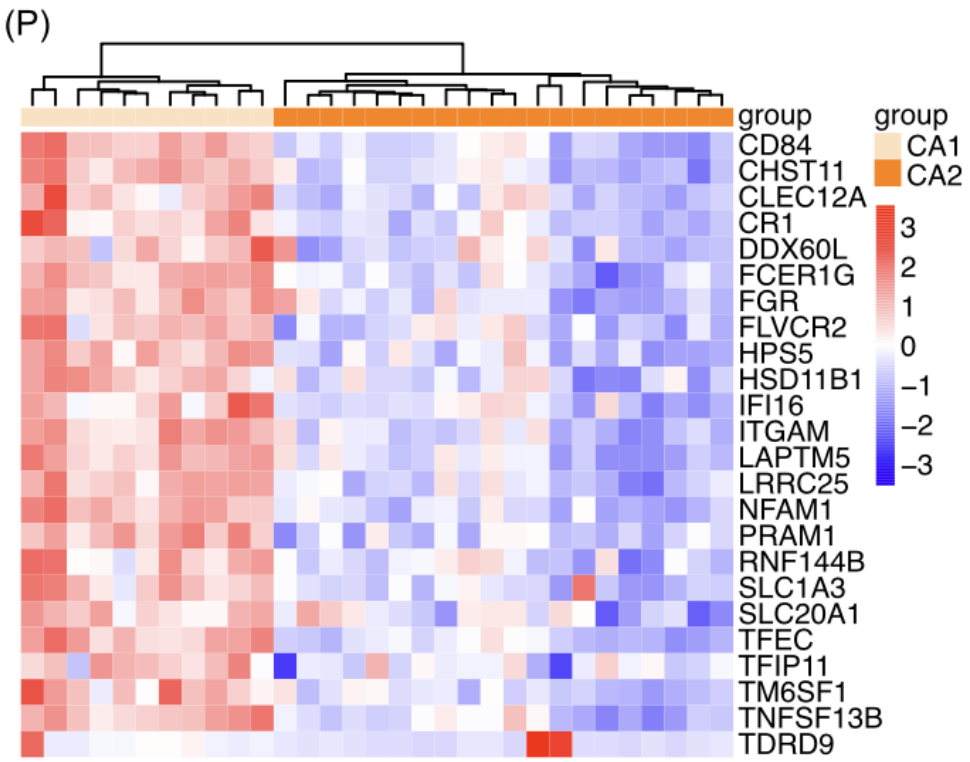
- **Immune Microenvironment:** The CA1 subtype exhibits high immune cell infiltration, accompanied by higher expression of exhaustion markers.

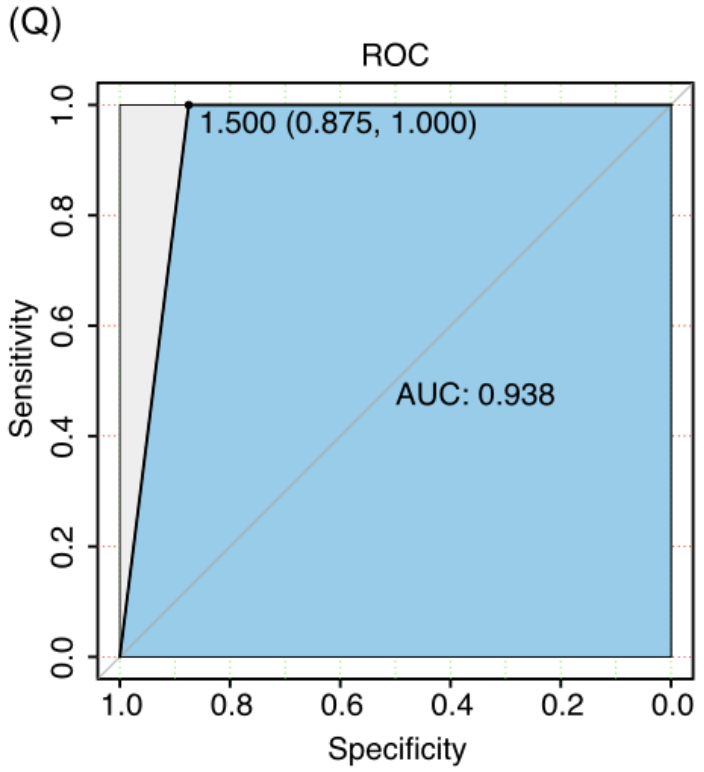
Subtype Features: Specific Microbes and Gene Enrichment

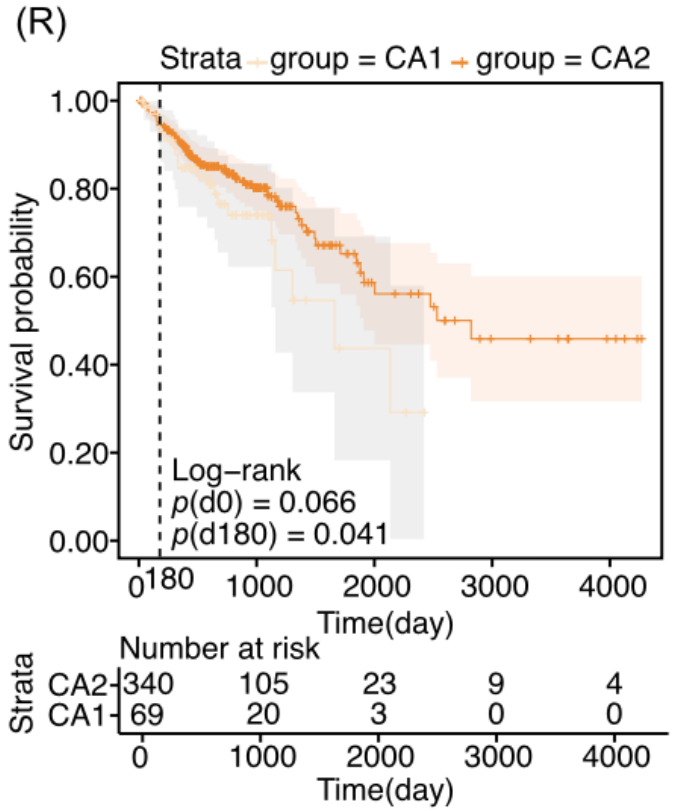


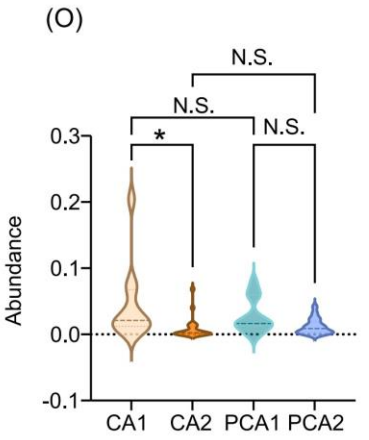
- **Key Microbiota:** *Porphyromonas gingivalis* and *Bacteroides fragilis* are significantly enriched in CA1.
- **Mechanism:** Upregulation of the GABA metabolic pathway promotes immune suppression.
- **Validation:** FISH experiments confirmed the in situ colonization of these bacteria in tumor tissues.

Random Forest-based Clinical Prediction Model and Validation



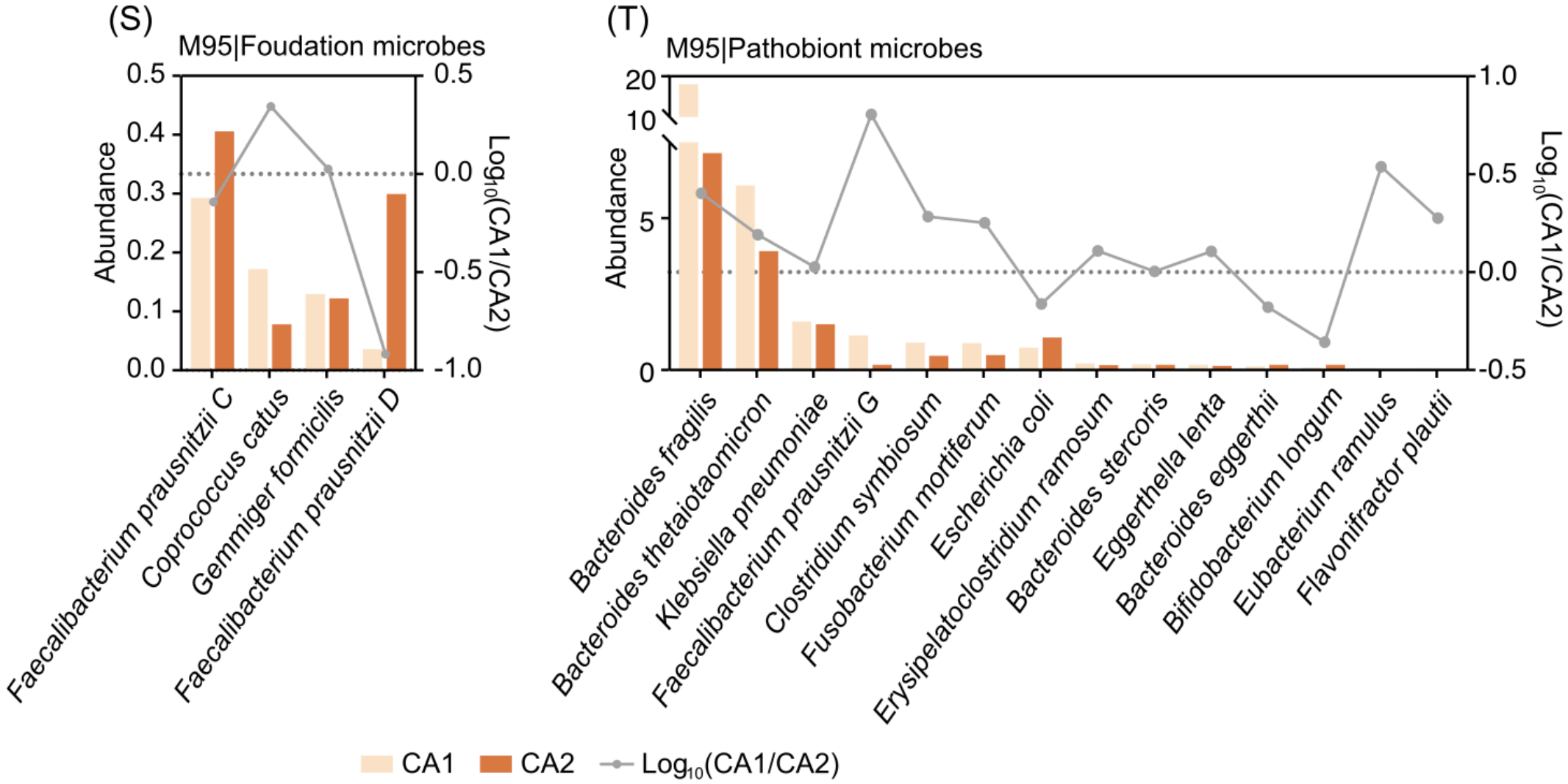






- **Model Construction:** Screened 24 feature genes to build a random forest classifier.
- **Accuracy:** AUC reached 0.938.

Cross-Cohort Validation



CA2 tumors are enriched with "healthy" foundation microbiota, while CA1 tumors are dominated by pathogenic pathobionts. (TCGA validation implies CA1-like patients have worse survival).

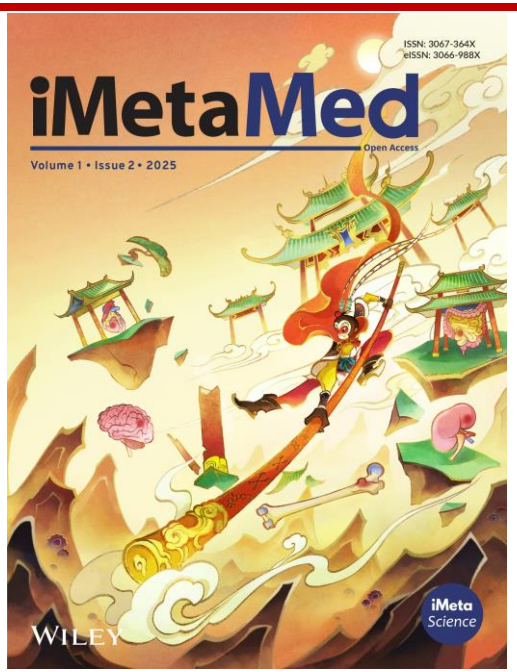
Summary

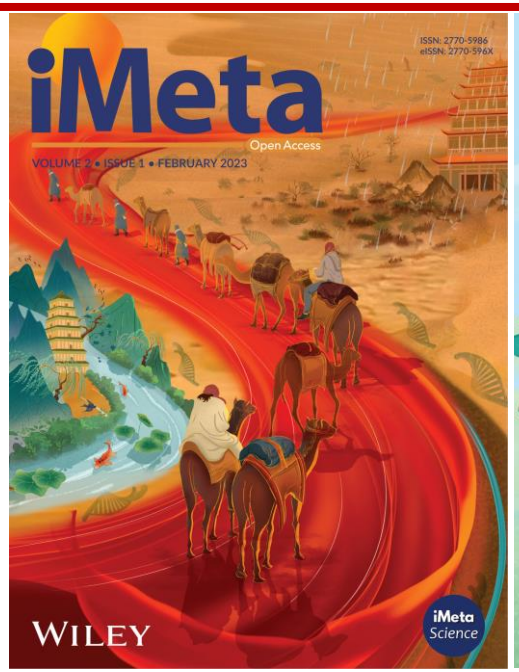
- **Integrated Subtyping:** Combined transcriptomics and in situ microbiomics to identify two CRC immune subtypes, CA1 and CA2.
- **Immune Features:** The CA1 subtype is characterized by high immune infiltration accompanied by immune exhaustion (high checkpoint expression) and poor prognosis.
- **Microbial Drivers:** *P. gingivalis* and *B. fragilis* may drive the formation of an immunosuppressive microenvironment through the GABA metabolic pathway.
- **Clinical Value:** The constructed 24-gene classification model can effectively predict patient prognosis, providing new strategies for targeted microbial adjuvant immunotherapy.

Shuting Xia, Likun Wang, Yangzhuo Xu, Jiaqi Zhang, Zeyang Zhou, Libing Sun, Heng Li, et al. 2025. Microbial Influences on Immune Modulation and Colorectal Cancer Progression Through Combined Transcriptomic and Microbiomic Analysis. ***iMetaOmics*** 2: e70072. https://doi.org/10.1002/imo2.70072

iMeta: To be top journals in biology and medicine

WILEY





"***iMeta***" launched in 2022 by iMeta Science Society, impact factor (IF) **33.2**, ranking top 65/22249 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 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 2025/7/6