

Gut Microbiota in Treating Inflammatory Digestive Diseases: Current Challenges and Therapeutic Opportunities

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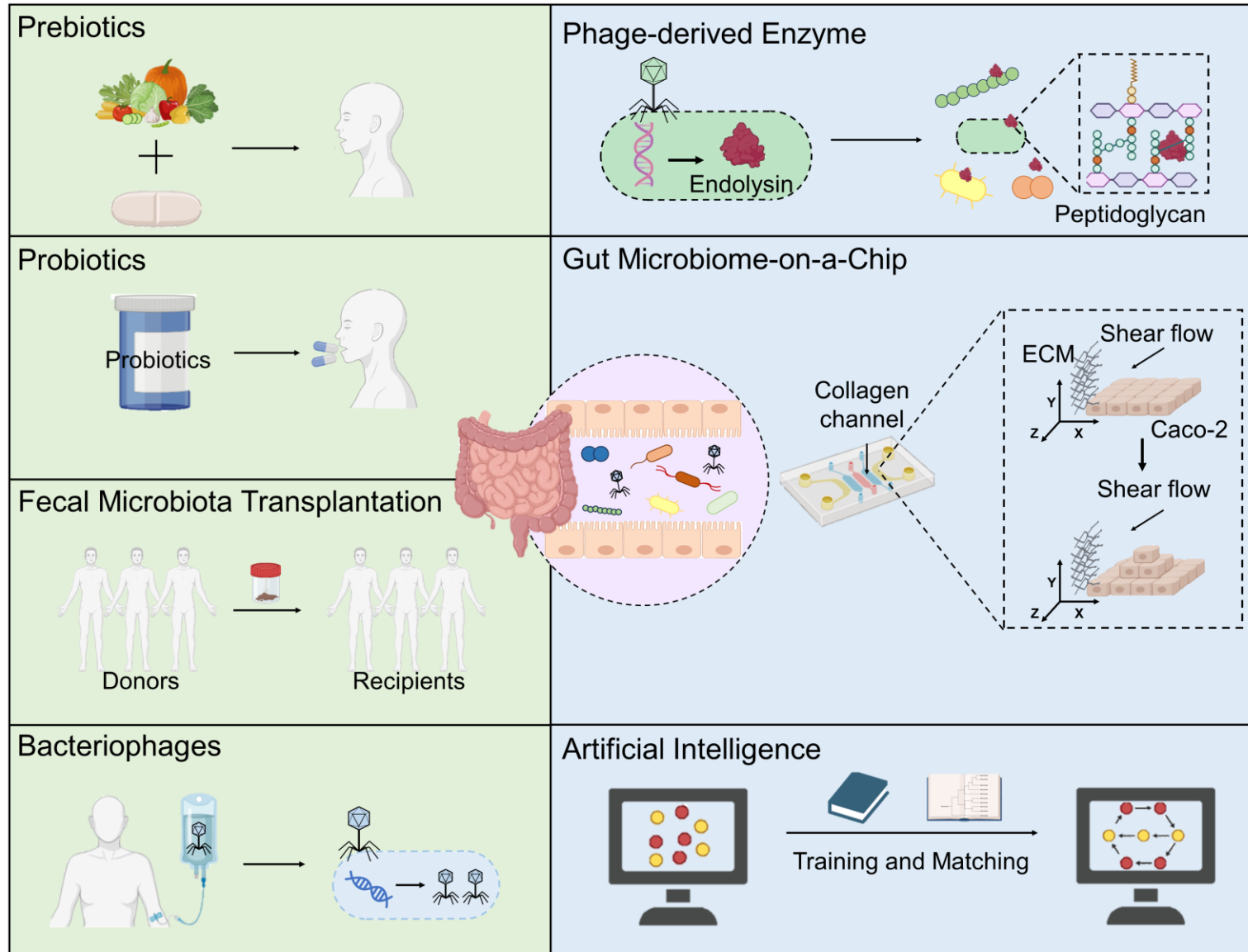
Challenges in exploring the role of the gut microbiota in inflammatory digestive diseases

- The gut microbiome compositions of patients exhibit considerable **heterogeneity** and contradictory findings across studies, presenting a significant challenge in current microbiota and inflammatory digestive disease research.
- **Incomplete metabolomic data** remains a major predicament, which is not only reflected in the scarcity of clinical metabolomic data for conditions like primary sclerosing cholangitis and acute pancreatitis, but also in the uncertainty of gut metabolite function.
- The majority of research has focused on alterations in gut bacteria within inflammatory digestive diseases and their influence on disease progression, while largely neglecting the role of the gut **mycobiome and virome-elements**.
- The resource competition and the selection pressure engendered by metabolic activity among microorganisms give rise to diverse **ecological interactions** not only within bacteria, but also between bacteria and fungi or viruses. How these interactions affect the development of inflammatory digestive diseases is a fascinating area.
- Microbial-based biomarkers have **limited diagnostic and predictive accuracy**.

Potential causes of heterogeneity in microbial composition of the same disease in different studies

Classification of causes	Interpretation
Sample bias	<ul style="list-style-type: none">※The timing of sample collection can affect the reproducibility of microbiome analyses even more than experimental interventions or dietary changes, and researchers should consider host circadian dynamics in experimental design.※The population exhibits considerable individual variability, and the sample size plays a crucial role in influencing the accuracy of the analysis and the reliability of the statistical results.※Fecal microbial load is a key factor driving gut microbiome variation and serves as a significant confounder in disease association studies.
Disease stage or subtype identification error	※Disease stage and subtype classification affect the results of microbiological analysis in a population cohort. For example, obese and lean MASLD patients may have significantly different gut microbiota, and mixed analyses may produce misleading results.
Individual factors	※Host genetic background, race, diet, drugs, and other variables can also cause differences in gut microbiota.
Sequencing techniques	<ul style="list-style-type: none">※16S rRNA gene sequencing is still the dominant method in current research, but the results are far less detailed and accurate than metagenomic sequencing, which can sequence the entire genome and produce more species information.※Primer's choice, reference databases, clustering methods, threshold setting, and specific processes can all cause taxonomic biases.
Sequencing regions	※The 16S rRNA gene sequence contains 10 conserved regions and 9 highly variable regions (V1-V9), but not every variable region has the same sensitivity. The selection of variable regions has a significant impact on the sequencing results of prokaryotic microbial community structure, with most studies ranging from a single variable region, such as V3 or V4, to two variable regions, such as V3-V4 or V4-V5, and some have three variable regions, such as V1-V3 or V4-V6.
Sequencing platforms	※The Illumina sequencing platform is widely used in microbiome studies with its lower cost advantages and higher throughput advantages, but the sequences produced by it are short (≤ 300 bases) and the resolution is limited.
Statistical bias	※P-values are often used to explain whether microbial abundance is statistically significant or not, however, P-values alone do not provide reliable results and require a false discovery rate (FDR) correction, which some studies do not.

Microbiota-based therapeutic strategies and emerging technologies



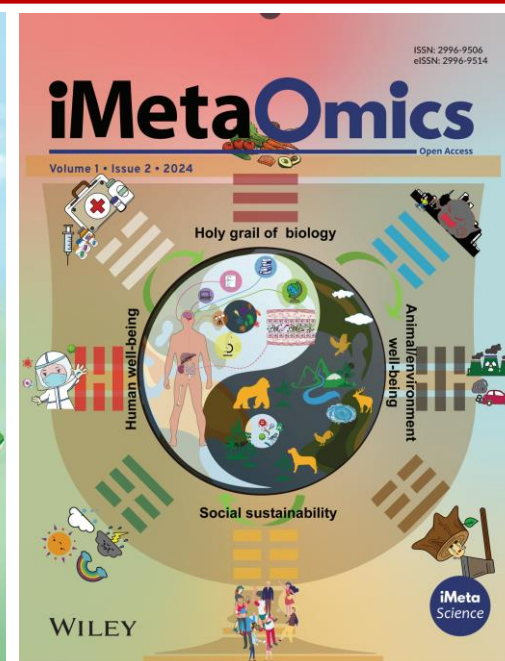
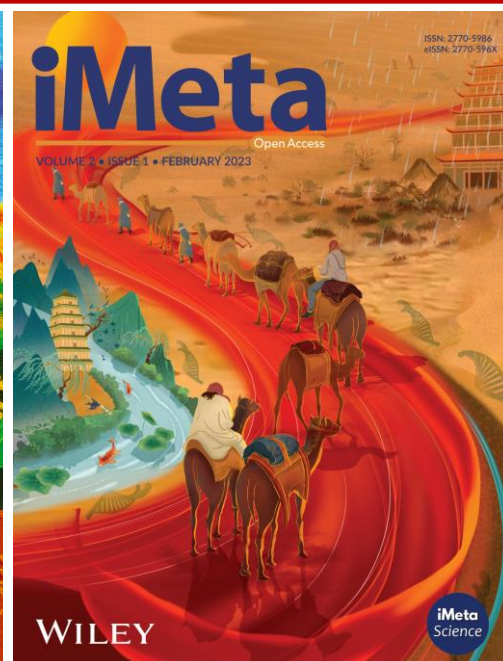
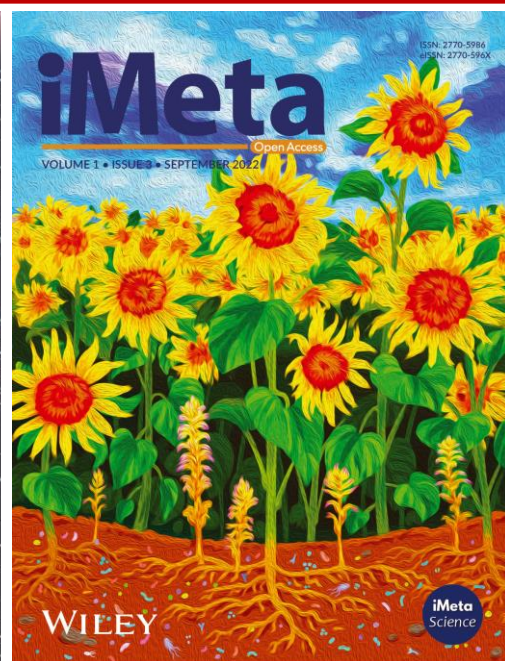
Existing Treatment Strategies

Emerging Strategies and Technologies

Summary

- ❑ Gut microbiota plays a crucial role in the development and progression of inflammatory digestive system diseases, and exploring the niche changes of gut microbiota provides new insights into its pathogenesis.
- ❑ The heterogeneity of microbial data, influenced by numerous confounding variables, remains a ubiquitous challenge in population cohort studies.
- ❑ Intervention strategies based on gut microbiota have promoted the clinical treatment of inflammatory digestive diseases, and emerging technologies and artificial intelligence are injecting new vitality into microbial-related therapies.

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