



Precision microbial regulation: strategies for modulating GIT microbiota for host health

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Introduction

Gastrointestinal microbes help hosts maintain physiological stability, promote growth, and control disease

Can microbes be precisely regulated to change towards a desired state?

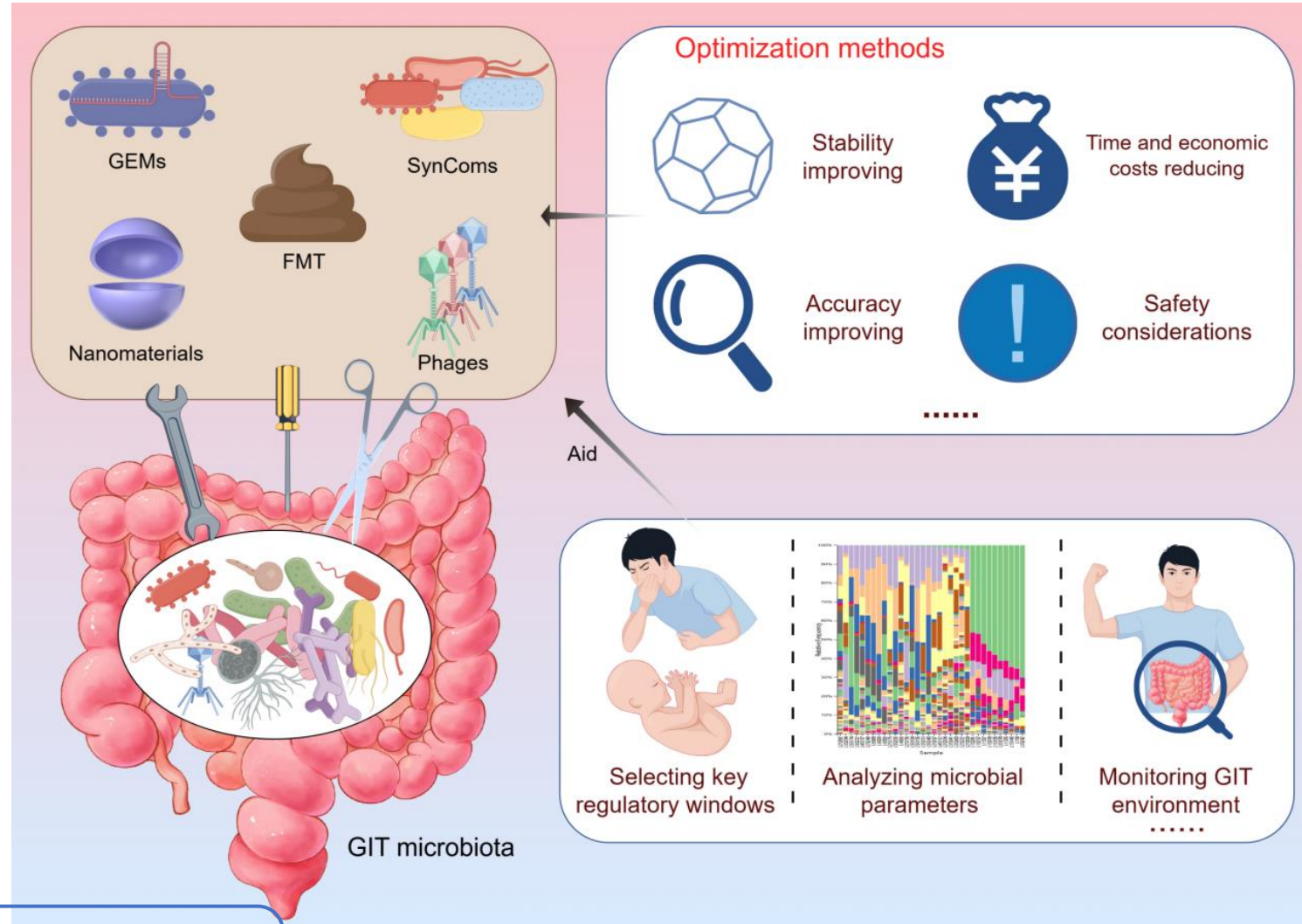
Fecal microbes transplants, synthetic microbial communities, gene-edited microbes, phages, nanomaterials, and other novel microbial regulatory strategies

What limits their practical application and how can they be solved?

Accuracy, stability, safety, economy optimization strategies

How can other microbiology knowledge aid microbial regulation?

Selecting regulatory windows, analyzing parameters to identify biomarkers, and monitoring the GIT environment





Highlight

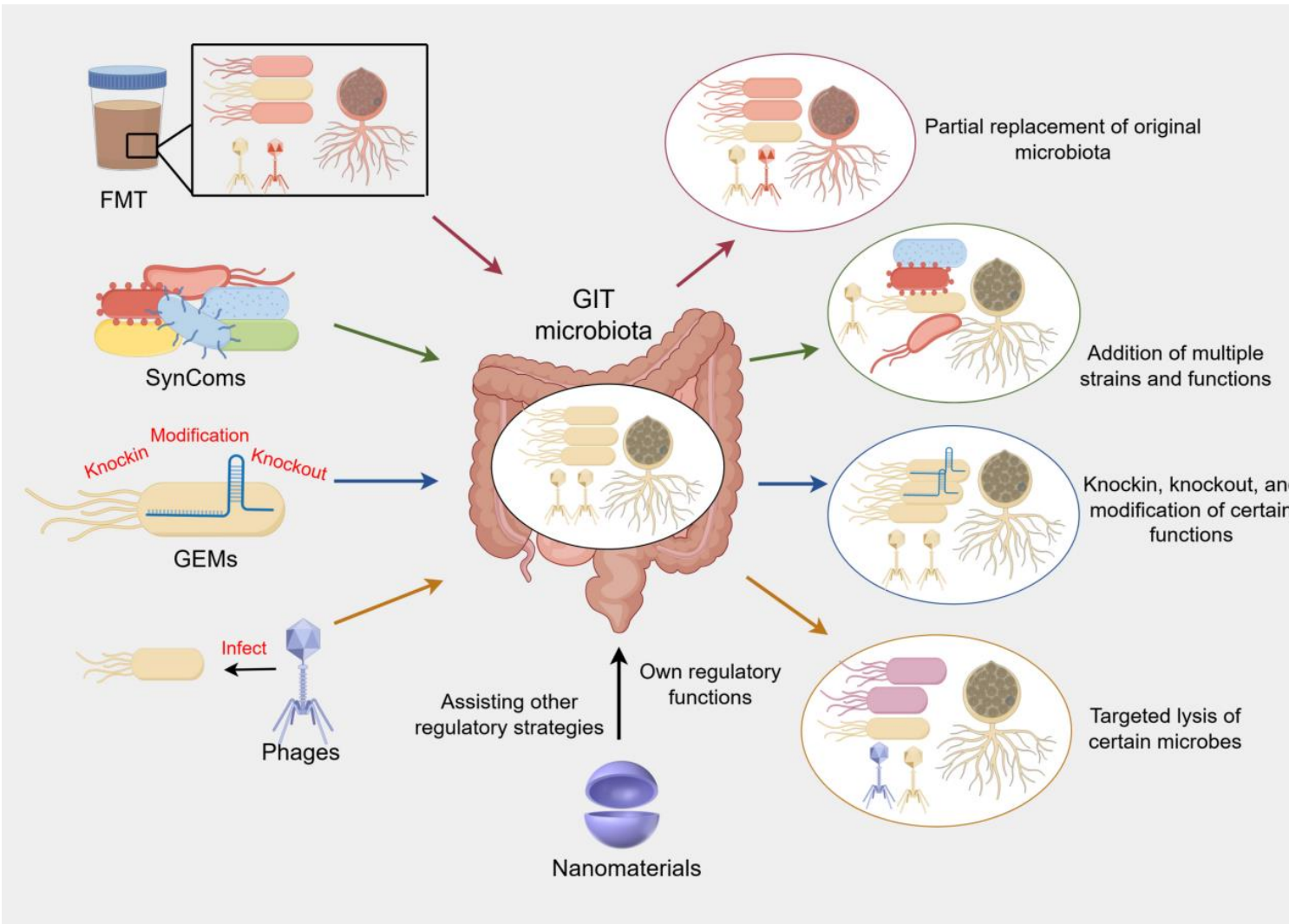


Figure 1 Targeted GIT microbial regulatory strategies and their characteristics



Emphasized the necessity of targeted strategies in regulating GIT microbiota.



The precise regulation strategies for GIT microbiota include FMT, SynComs, GEMs, phages, and nanomaterials, all of which have been individually reviewed.



Equipping these strategies with more microbiological discoveries will help improve the precision of selecting intervention timing and microbial biomarkers.



Targeted Regulatory Strategies for GIT Microbiota

Many factors influence GIT microbes, and in addition to genetic and environmental factors, antibiotics, probiotics, prebiotics, synbiotics, and postbiotics have been developed as modulatory strategies.

Genetic, environmental are difficult to control; antibiotic use may lead to dysbiosis; the effectiveness of probiotic products is not stable; simple supplementation with probiotics is difficult to accurately regulate GIT microbiota

FMT

SymComs

GEMs

Phages

Nanomaterials

Mechanisms

Safety

Effectiveness

Clinical effects

Optimization strategies

Table 1 Several clinical trials on targeted regulation approaches conducted within the past five years

Situation	Method	Outcome	Year	NO.	Ref.
CDI	FMT (spores)	Reduced the risk of recurrent infections with a good safety profile	2022	NCT03183128	[192]
CDI	FMT	Improved both the physical and psychological condition of the patients	2023	NCT03244644	[193]
SLE	FMT	Improved systemic immune-inflammation profiles	2022	ChiCTR2000036352	[194]
ASD	FMT	Decreased 5-HT and GABA levels in serum, and alleviated ASD	2021	ChiCTR1800014745	[195]
CDI	SynCom	High-dose SynCom prevented the recurrence of CDI	2023	NCT03788434	[196]
CDI	SynCom	Among the 19 patients, 16 (84%) had no recurrence by day 130	2021	NCT02865616	[197]
Advanced Solid tumors	SynCom	SynCom are tolerable and safe in ICI recipients, regardless of tumor type, and may influence the microbiota and metabolites	2023	NCT03686202	[198]
PKU	GEM	Safe and well-tolerated; a dose-responsive increase in strain-specific phenylalanine metabolites was observed	2021	NCT03516487	[199]
PKU	GEM	GEM metabolize phenylalanine in the gut, reducing postprandial plasma and fasting plasma phenylalanine levels in PKU patients	2023	NCT04534842	[200]
T1D	GEM	The frequency of proinsulin-specific CD8 ⁺ T cells decreased	2023	NCT03751007	[201]
Hyperammonemia	GEM	GEM can metabolize ammonia and produce nitrate, leading to a significant dose-dependent increase in 15 N-nitrate levels in urine and plasma	2019	NCT03179878	[80]
IBD	Phage	With good safety and tolerance and could survive in GIT	2022	NCT04737876	[21]
消化道 issues	Phage	Fecal <i>E. coli</i> load was reduced, along with a decrease in IL-4 levels	2019	NCT03269617	[202]
ICD	Phage	In progress	2021	NCT03808103	[203]
Metabolic syndrome	FVT (FFT)	Influenced the composition of phages in GIT, with good safety and tolerability	2023	NL8289	[204]



Targeted Regulatory Strategies for GIT Microbiota

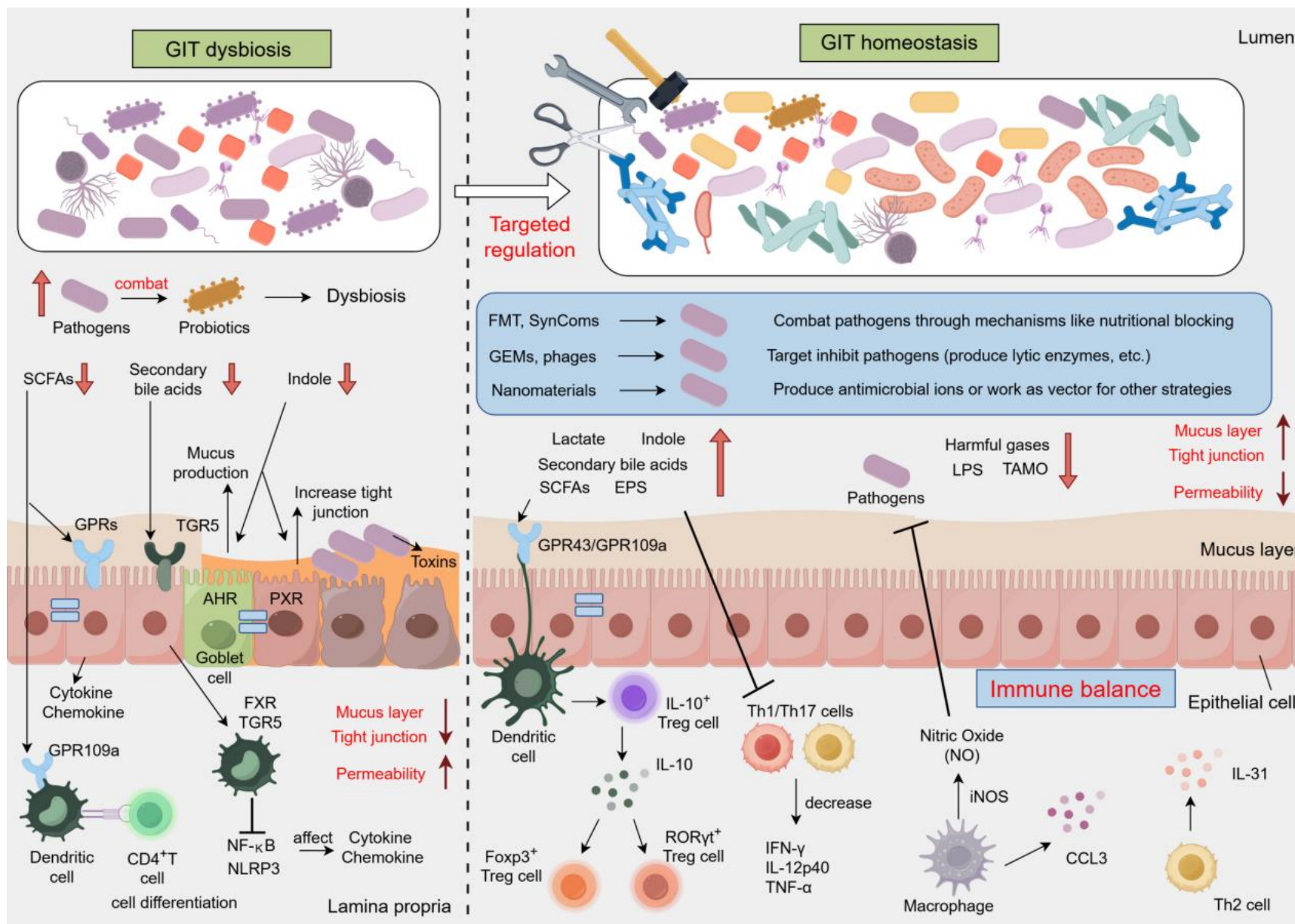


Figure 2 Microbial regulatory strategies can maintain GIT homeostasis



Optimization of Targeted Modulation Strategies for GIT Microbiota



Microbial modulation strategies need to be further optimized to improve precision, enhance stability, ensure safety, and reduce time and economic costs. These efforts will provide a solid foundation for their eventual widespread application.



Leveraging Microbial Knowledge to Aid Targeted Modulation Strategies

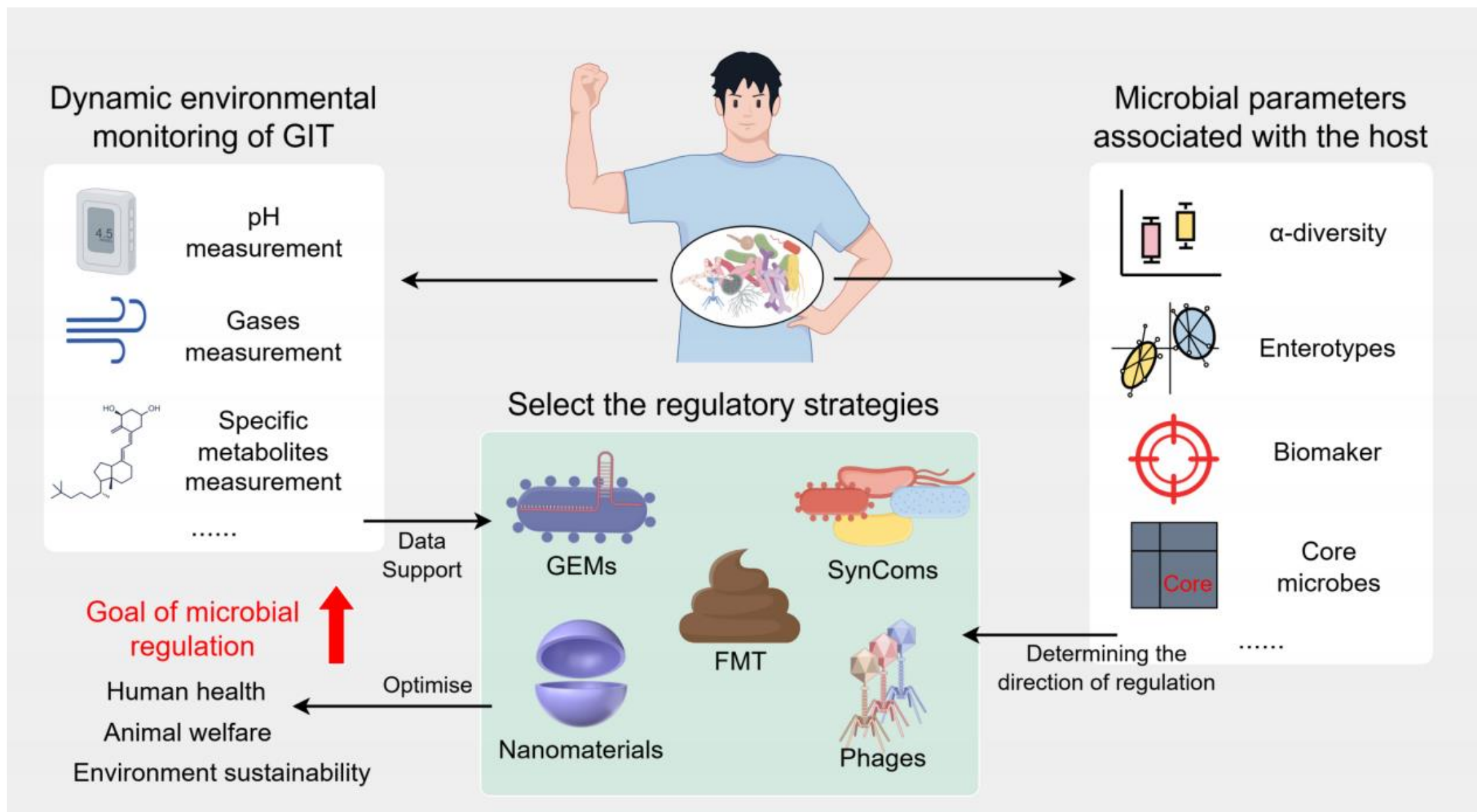


Figure 3 Support methods for regulatory strategies



Conclusion

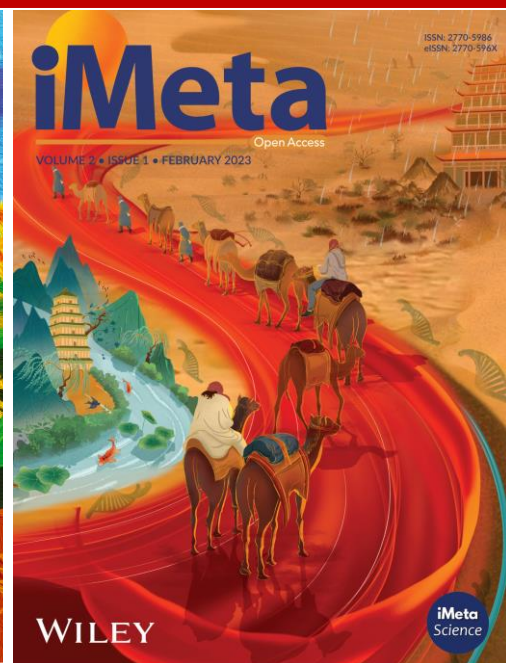
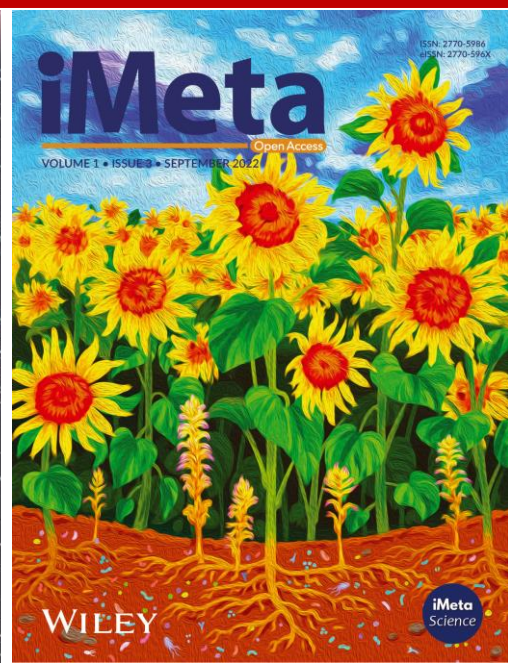
- ❑ This article explores the possibility of using targeted GIT microbial modulation strategies to promote host health and reviews the mechanisms, effectiveness, safety, and clinical outcomes of these strategies. The study suggests that fecal microbes transplants, synthetic microbial communities, genetically engineered microbes, phages, and nanomaterials are expected to be the next generation of GIT microbial modulation strategies.
- ❑ Optimizing the effectiveness, stability, safety, and economics of these strategies will help to apply them in real-world situations for targeted impact on GIT microbes.
- ❑ Cutting-edge microbial knowledge will aid in the use of regulatory strategies such as selecting microbial regulatory windows, identifying marker microbes as regulatory targets, and monitoring the GIT environment to capture regulatory timing.

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