Gut microbiota and tuberculosis

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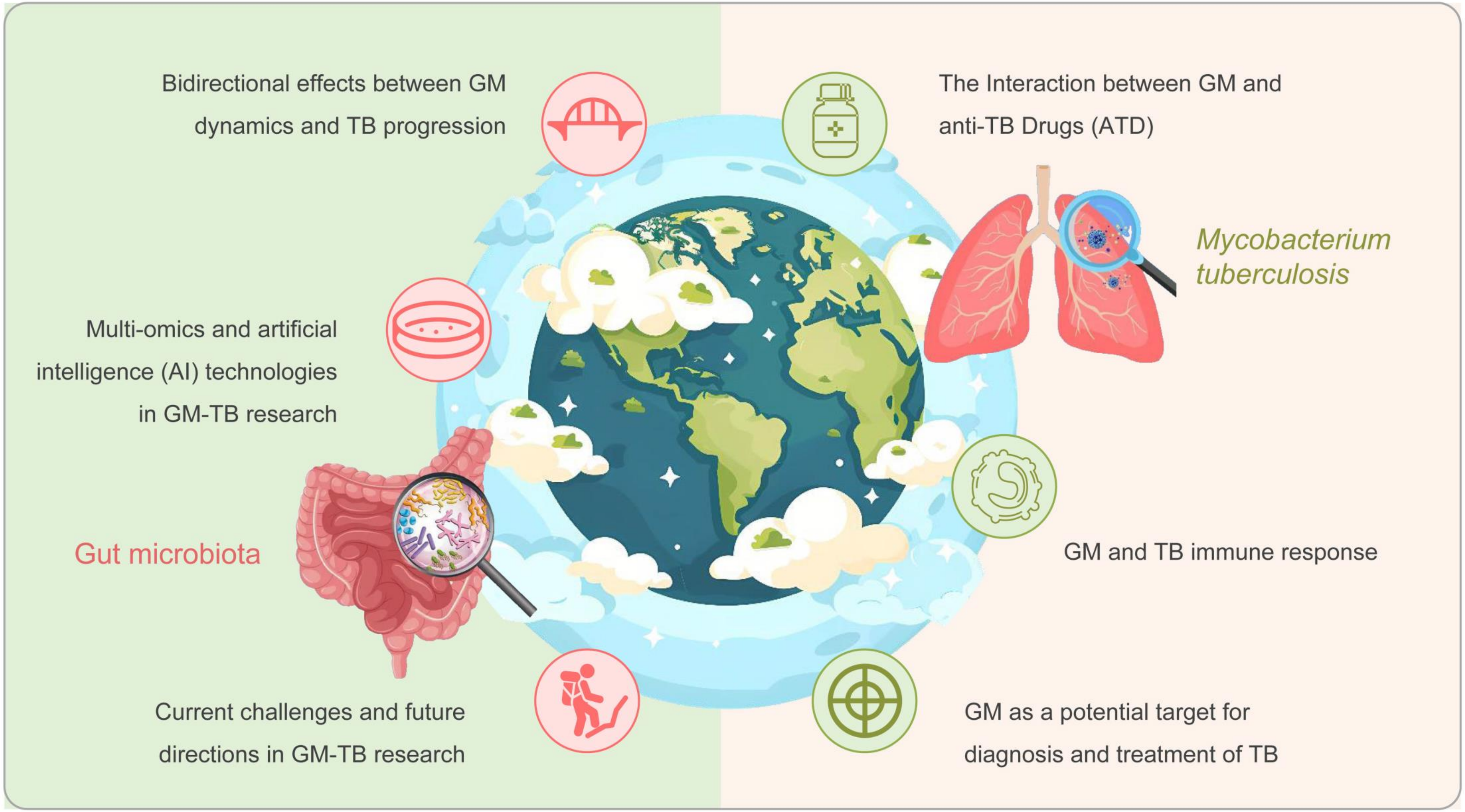
Yanhua Liu, Ling Yang, Maryam Meskini, Anjana Goel, Monique Opperman, Sagar Singh Shyamal, et al. 2025. Gut microbiota and tuberculosis. ***iMeta*** 4: e70054. https://doi.org/10.1002/imt2.70054.

Graphical Abstract

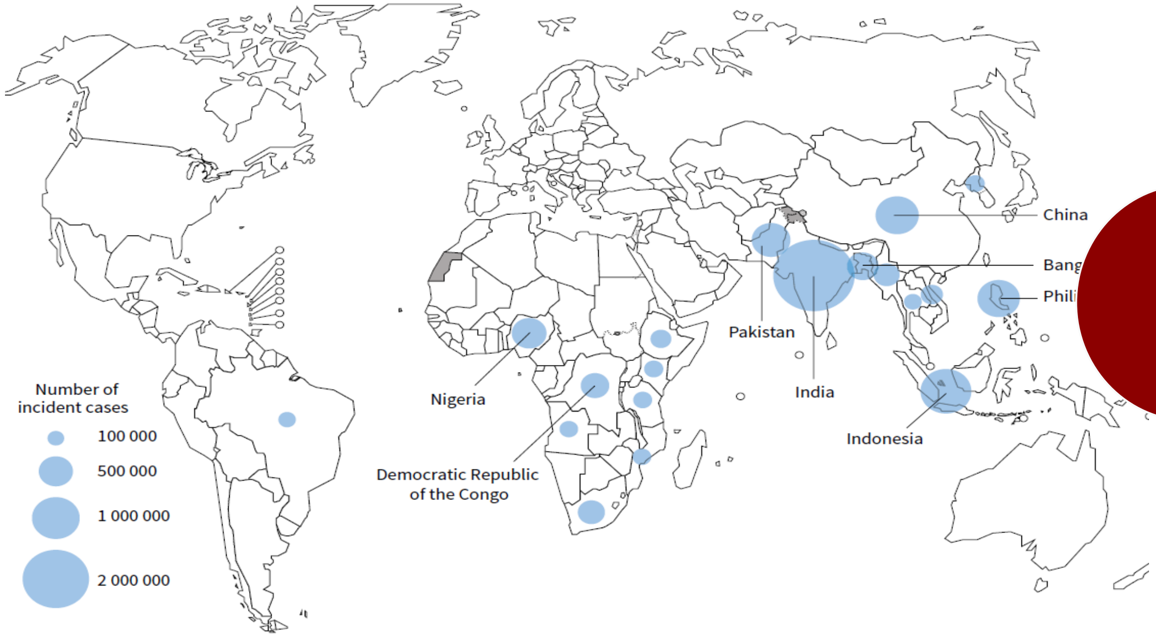


Highlights

- Bidirectional gut microbiota (GM)-tuberculosis (TB) interaction reveals a dynamic interplay where *Mycobacterium tuberculosis* infection disrupts GM, while GM dysbiosis exacerbates TB progression by modulating host immunity.
- Technological innovation integrates next-generation sequencing, metagenomics, and artificial intelligence (AI) to unravel complex GM-TB relationships, enabling predictive modeling and precision medicine approaches.
- Regarding GM as a diagnostic/therapeutic target, researchers propose GM modulation as a novel strategy to enhance anti-TB drug efficacy, mitigate side effects, and develop microbiome-based diagnostics for TB susceptibility and prognosis.
- A comprehensive research framework systematically synthesizes seven key areas—from GM-immune crosstalk to recurrence mechanisms—providing a roadmap for future TB management strategies and vaccine optimization.

Introduction

TB: leading infectious killer



New Tb Cases
10.7 Million

Tb-associated Deaths
1.25 Million

Co-infection Of HIV-MTBC
161,000 deaths

♣ *Global tuberculosis report 2024. Geneva: WHO; 2024.*

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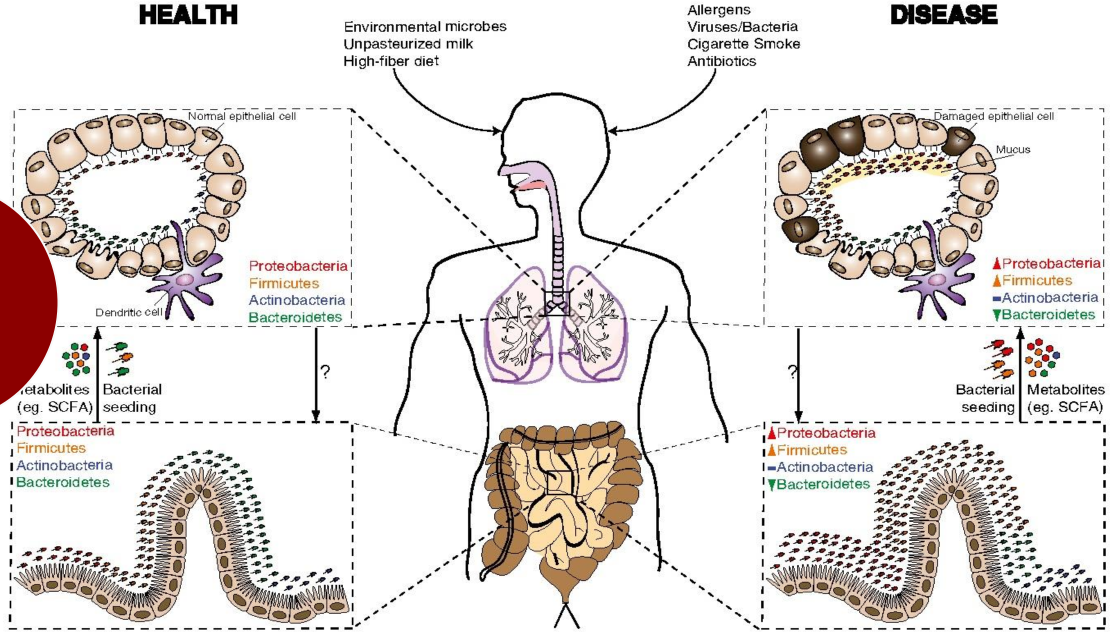
Gut-Lung axis



Intestinal-pulmonary cross-talk during respiratory health and disease

♣ *Marsland BJ. et al. Ann Am Thorac Soc. 2015.12, S150-156*

Bidirectional Effects Between GM Dynamics and TB Progression

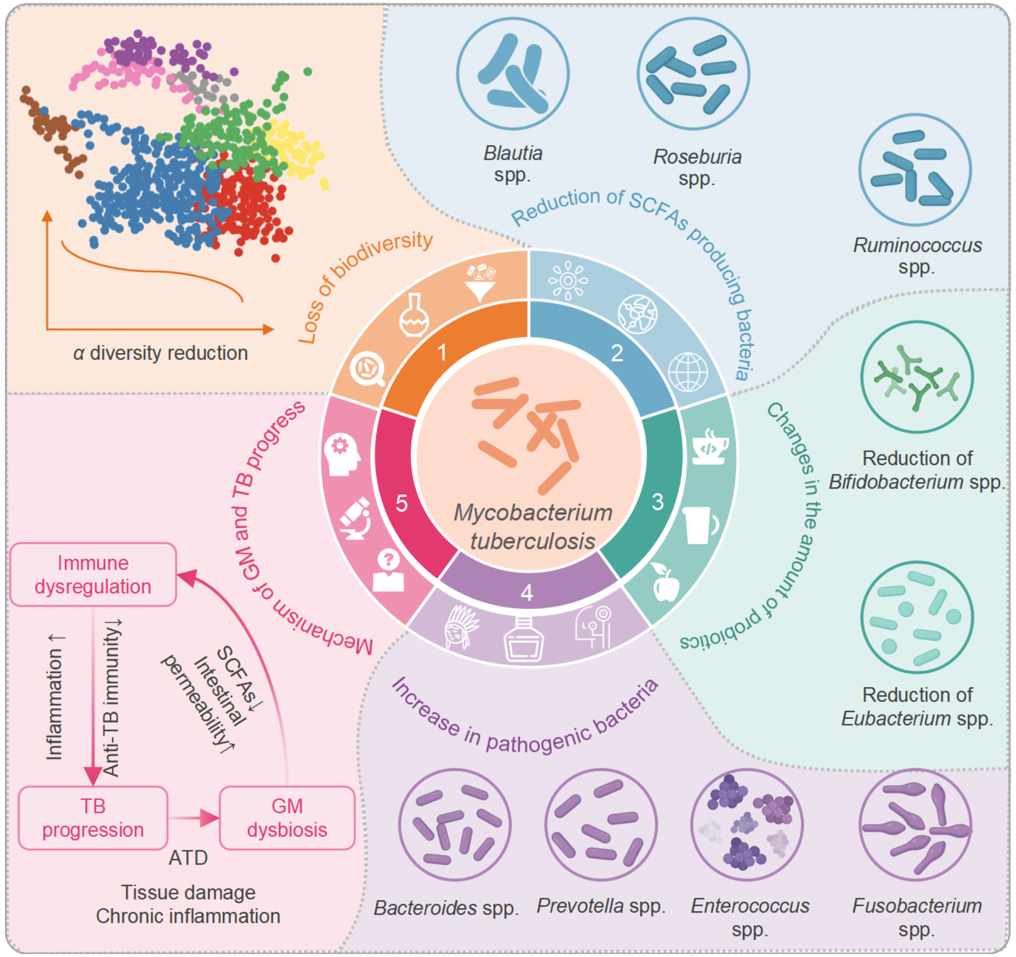


Figure 1 Relationship between GM dysbiosis and TB progression

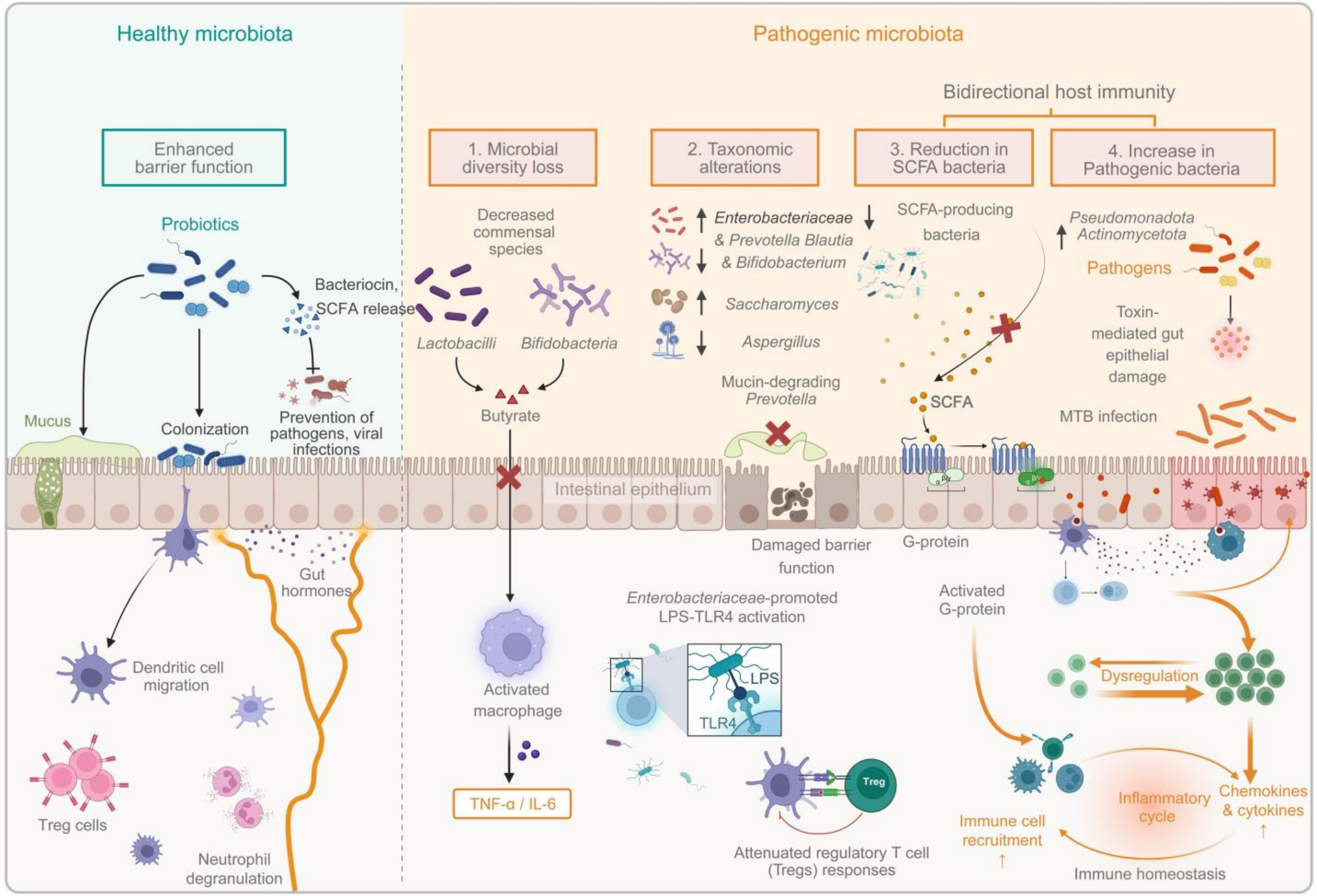


Figure 2 Comparative characterization of healthy versus pathogenic gut microbiota states

Bidirectional interactions between ATD and GM

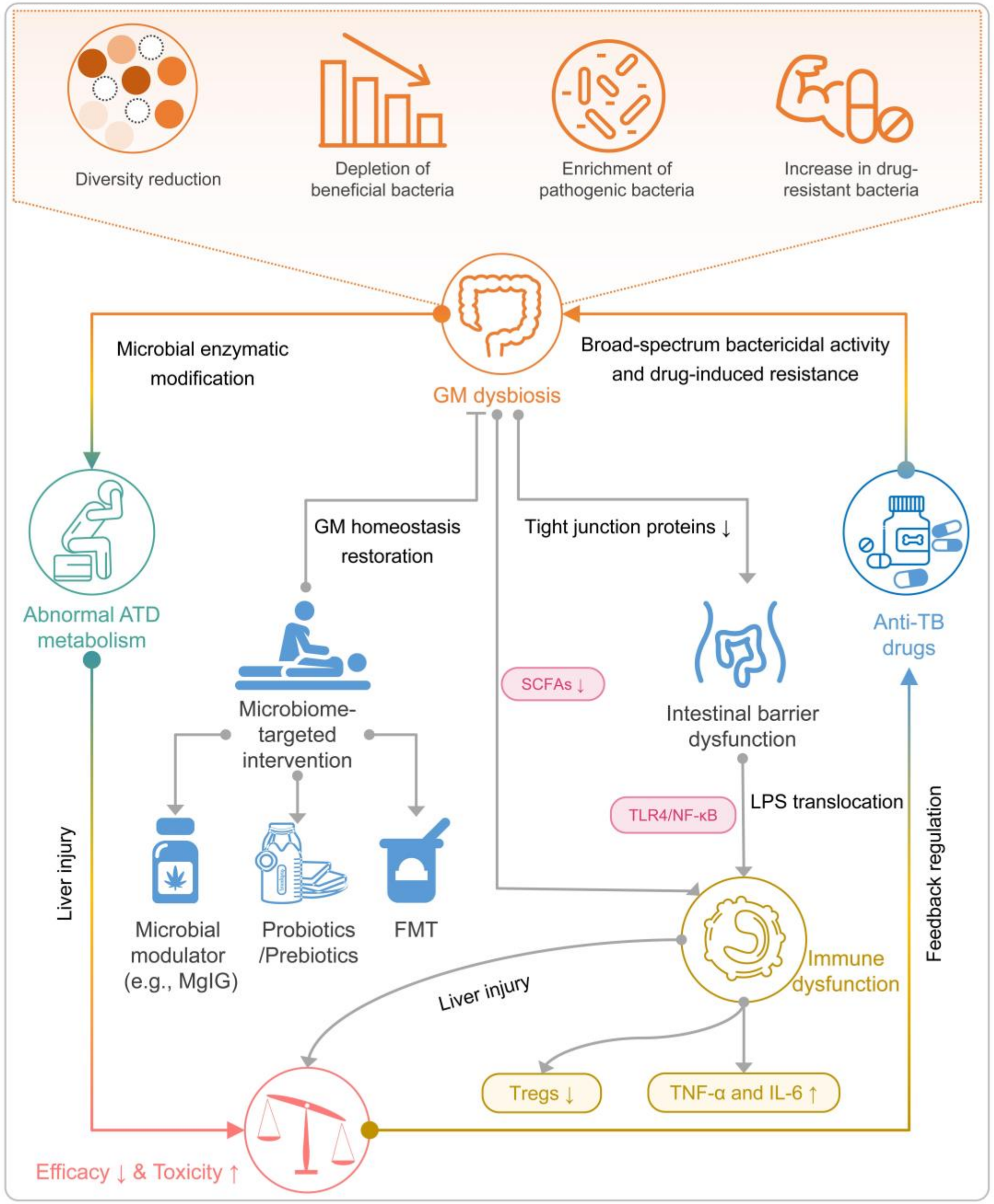


Figure 3 Bidirectional interactions between ATD and GM, and their impact on GM homeostasis.

◆ Impact of ATD on GM

Induces intestinal inflammation, destroys the gut barrier, disrupts metabolism, and directly kills bacteria→ damage to the composition and function of GM.

◆ Influence of GM on ATD metabolism

Abnormal drug metabolism and reduced bioavailability→ decreased efficacy; impaired immune regulation and increased hepatotoxicity→ exacerbated toxicity.

◆ Intervention strategies

Probiotics/prebiotics, magnesium isoglycyrrhinate (MgIG), fecal microbiota transplantation (FMT)→ anti - inflammatory, repair gut barrier, restore microbiome balance.

The Interaction Between GM and anti-TB drugs (ATD)

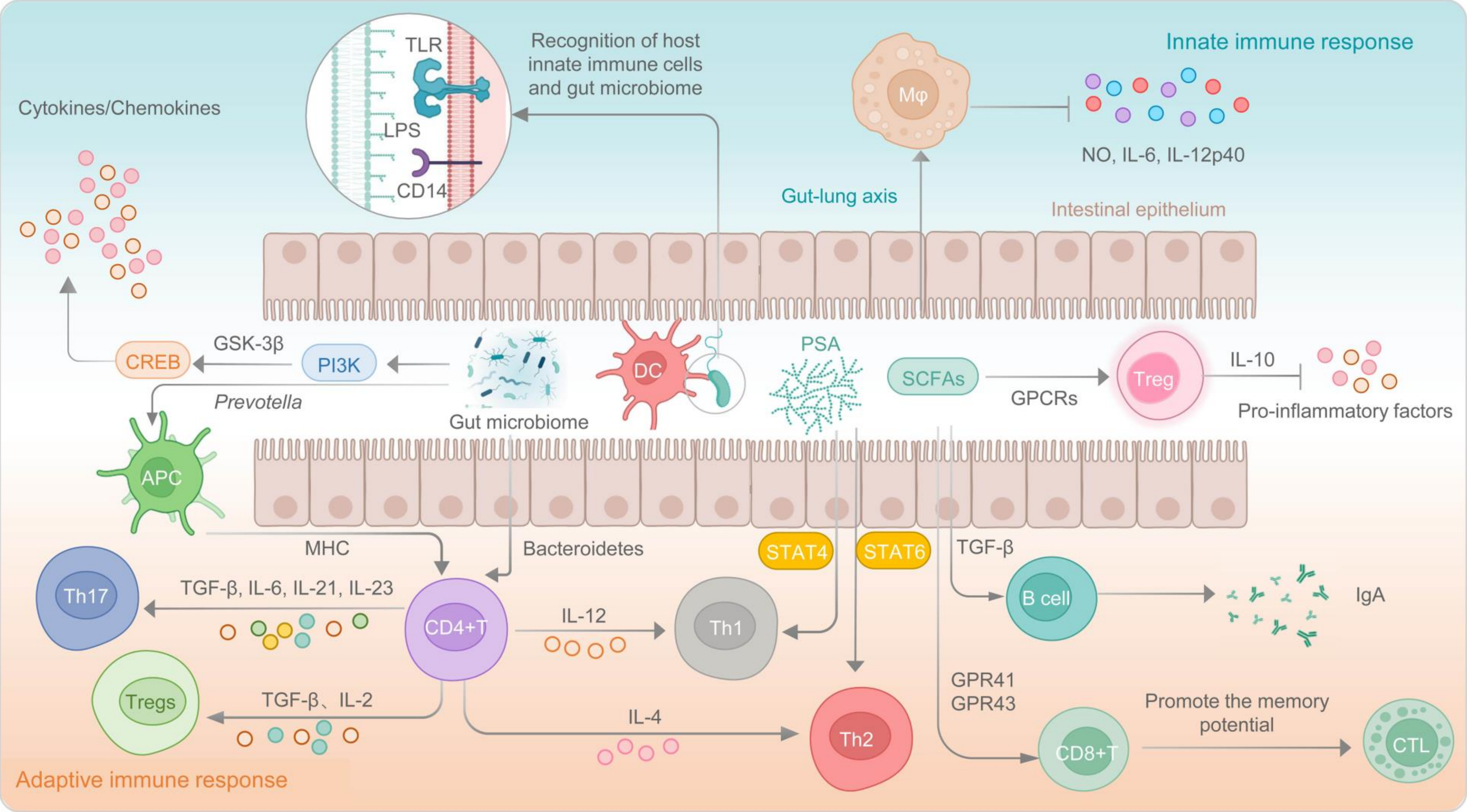


Figure 4 Multimodal regulation of host immunity by the GM

Gut Microbiota Regulates Immunity via Metabolites

- **Healthy GM Functions**:
  Maintains mucosal barrier and immune homeostasis
- **Metabolite Effects**:
  SCFAs regulate macrophage activity & Treg differentiation to suppress hyperinflammation
  Polysaccharide A modulates B/T-cell immune responses

Dysbiosis Exacerbates TB Pathology

- **Immune Dysregulation**:
  Th1/Th2/Th17/Treg imbalance → Impaired anti-MTB immunity
- **Gut-Lung Axis**:
  Gut dysbiosis triggers systemic inflammation → ↑MTB infection/relapse risk via gut-lung axis

GM as a Potential Target for Diagnosis and Treatment of TB

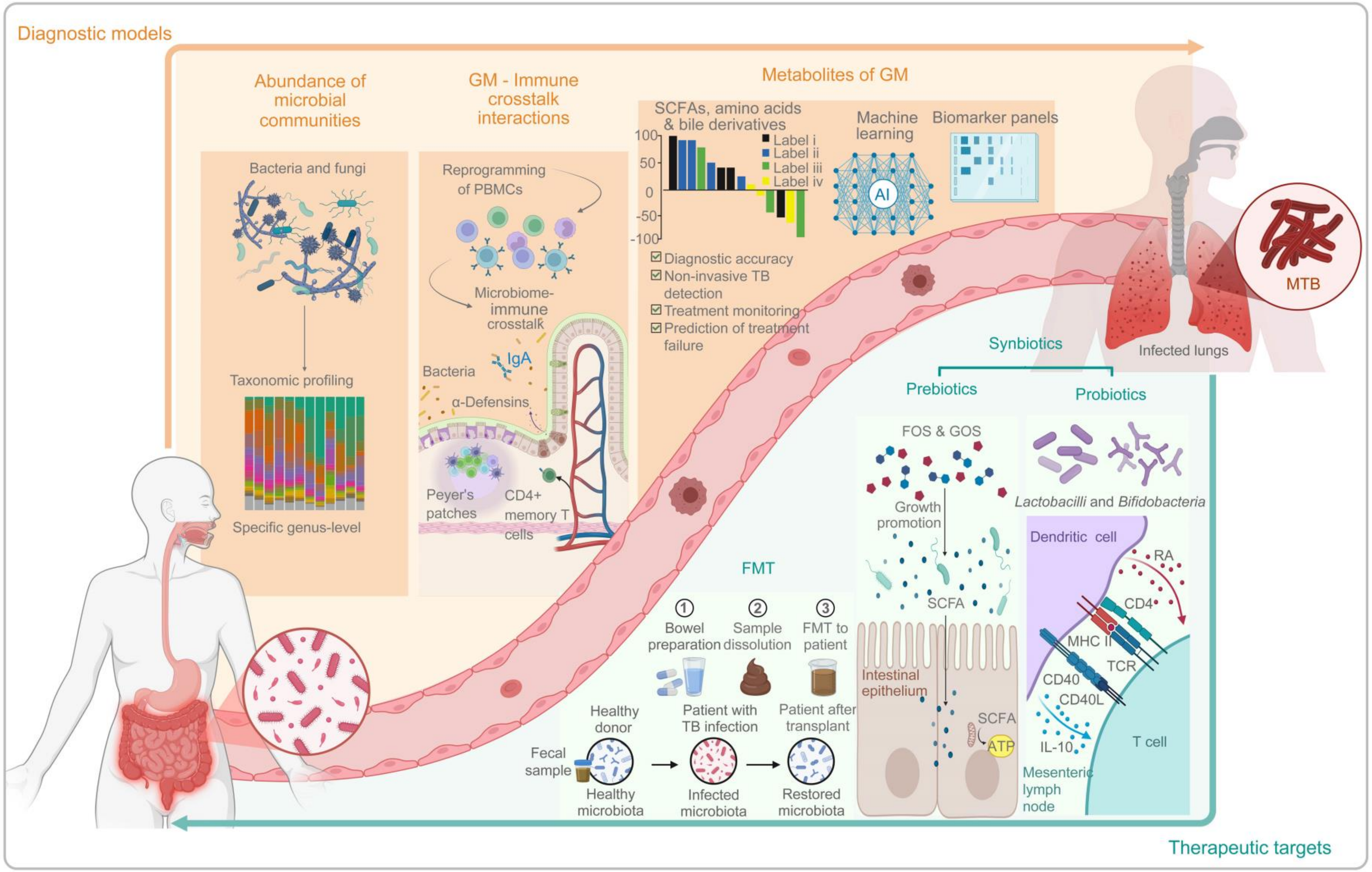


Figure 5 GM as a diagnostic and therapeutic target in TB

◆ The Pathogenic Role of GM

GM is a key regulatory factor in the development of TB, and its imbalance is closely related to disease progression, serving as a potential new target for diagnosis and treatment.

◆ Diagnostic Potential

Changes in microbial composition, fungal-bacterial interactions, and metabolite profiles participate in TB pathology through systemic circulation, offering early diagnostic value.

◆ Targeted Treatment Strategy

Probiotics, prebiotics, synbiotics, and FMT (Fecal Microbiota Transplantation) regulate the homeostasis of the microbiota, reduce complications from treatment, and serve as a targeted treatment strategy for TB. The mechanism includes restoring the intestinal barrier and improving immune function.

◆ Core Value

GM provides a dual intervention approach for the accurate diagnosis and treatment of TB, promoting innovation in the diagnosis and treatment of infectious diseases.

Application of Multi-omics and AI Technologies in GM-TB Research

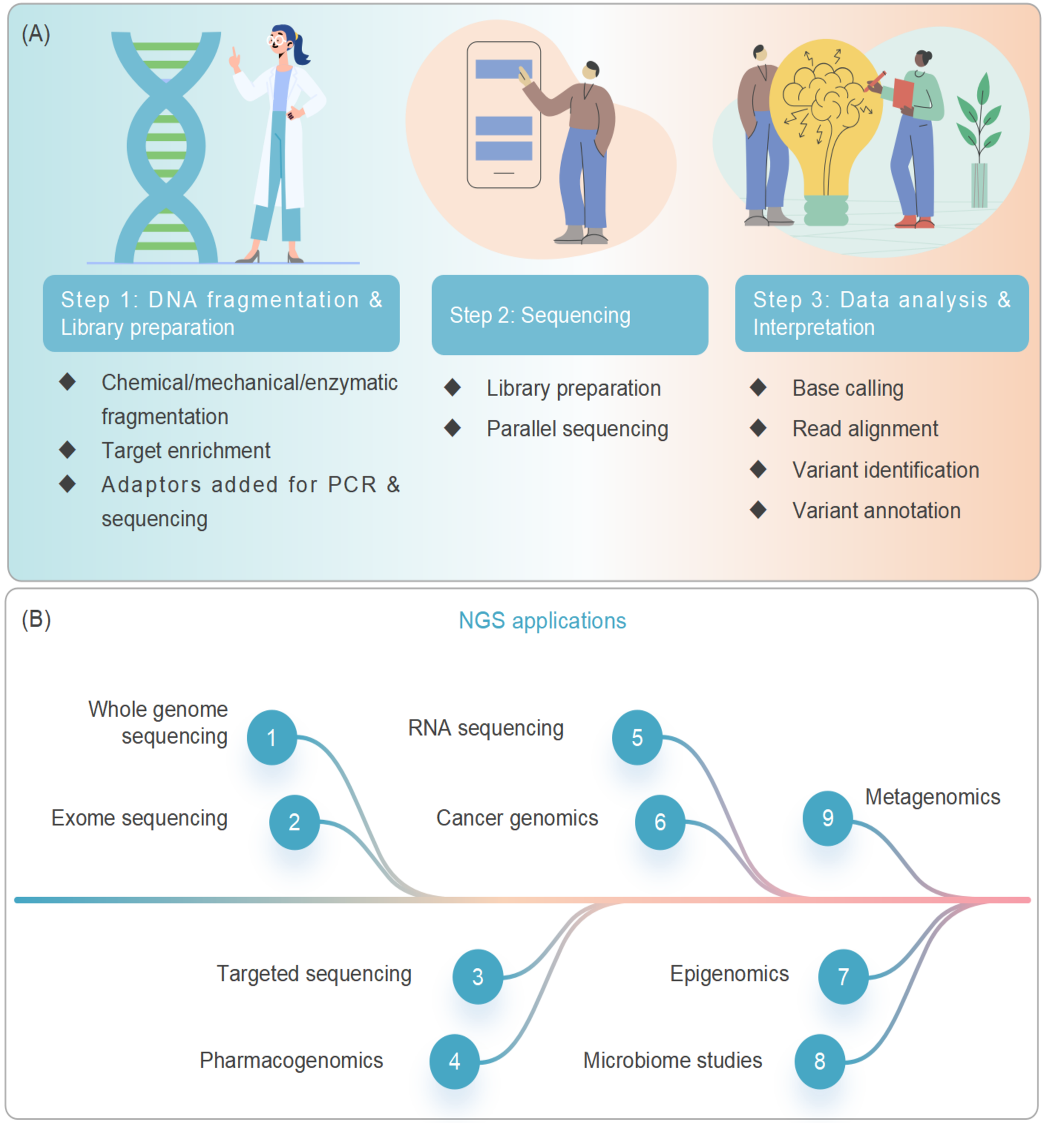
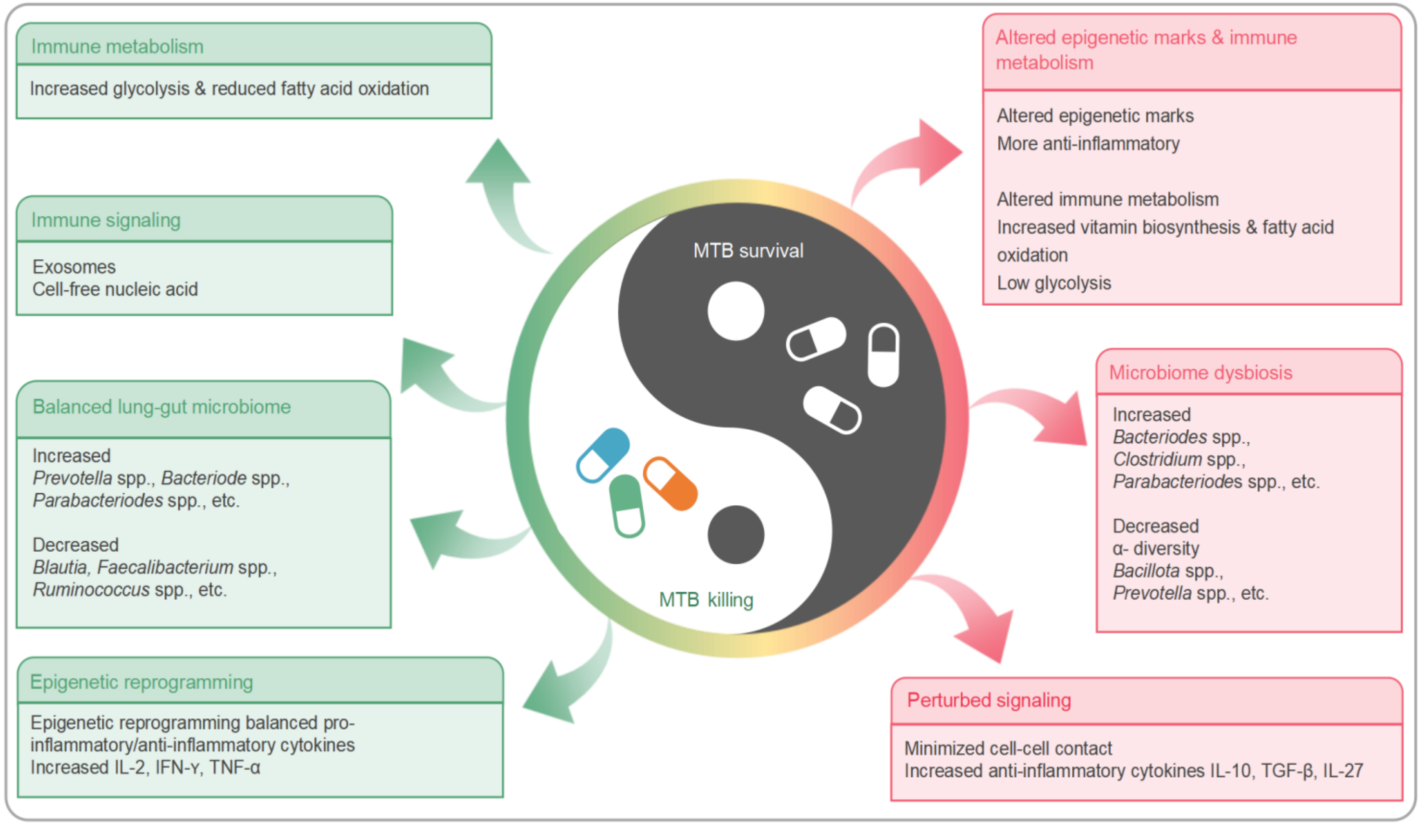


Figure 6 Overview of the next-generation sequencing (NGS) workflow and its applications.

Figure 7 Applications of NGS in GM-TB research.

Application of Multi-omics and AI Technologies in GM-TB Research

Figure 8 An overview of the host-microbe interactions and proteomics in TB progression



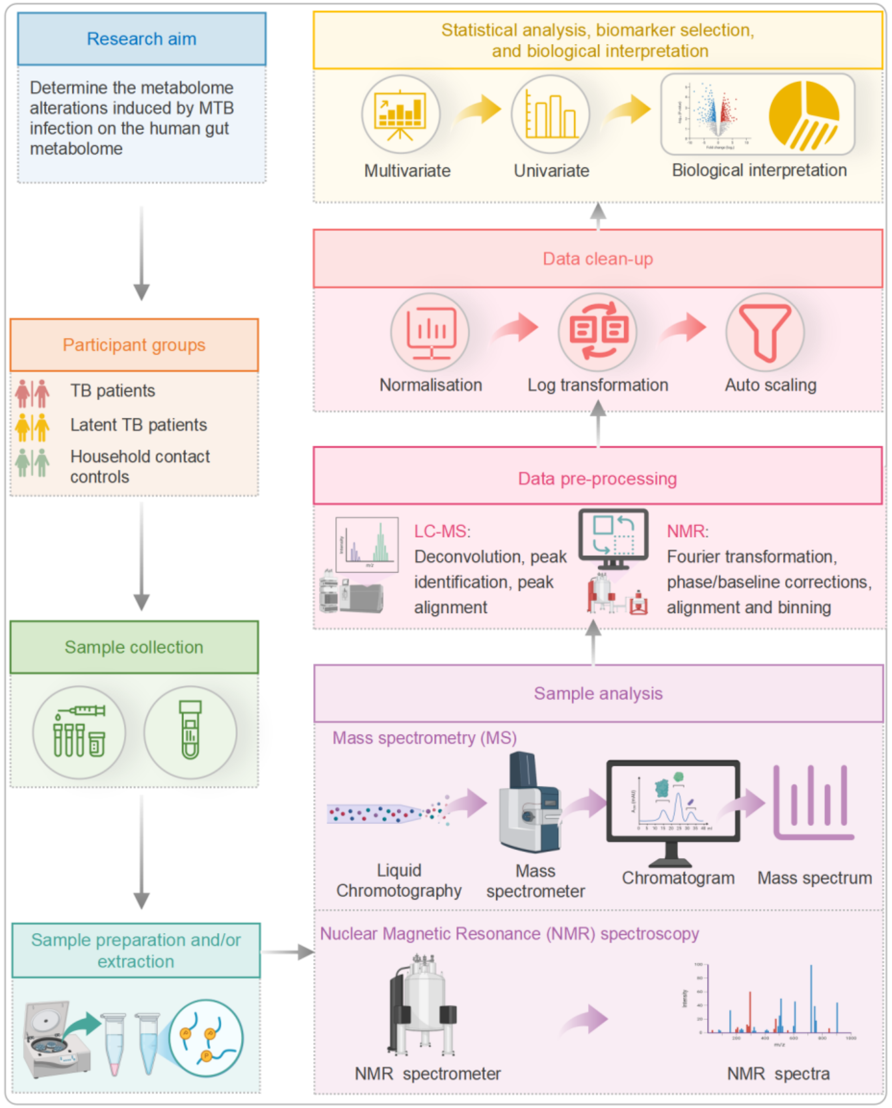


Figure 9 Overview of the general metabolomics workflow

Application of Multi-omics and AI Technologies in GM-TB Research

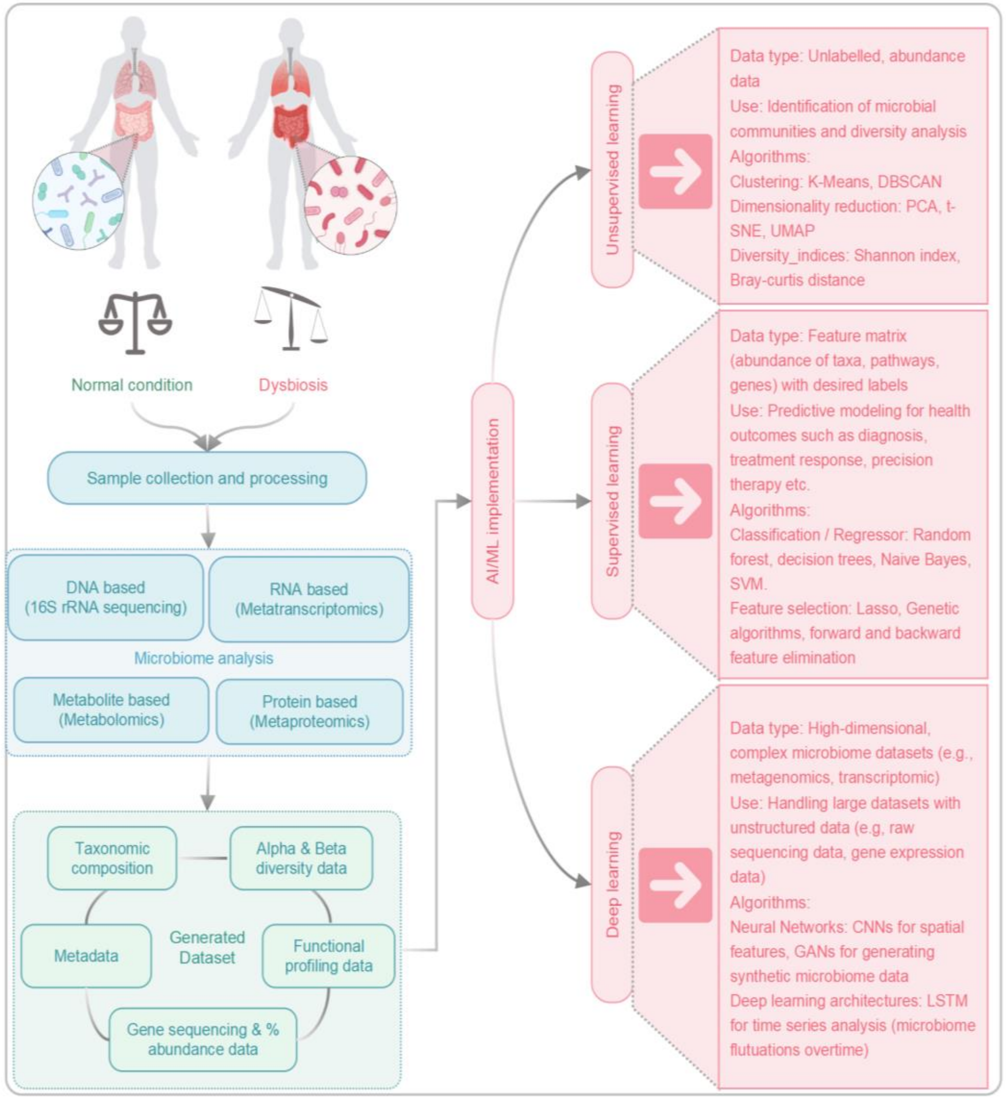
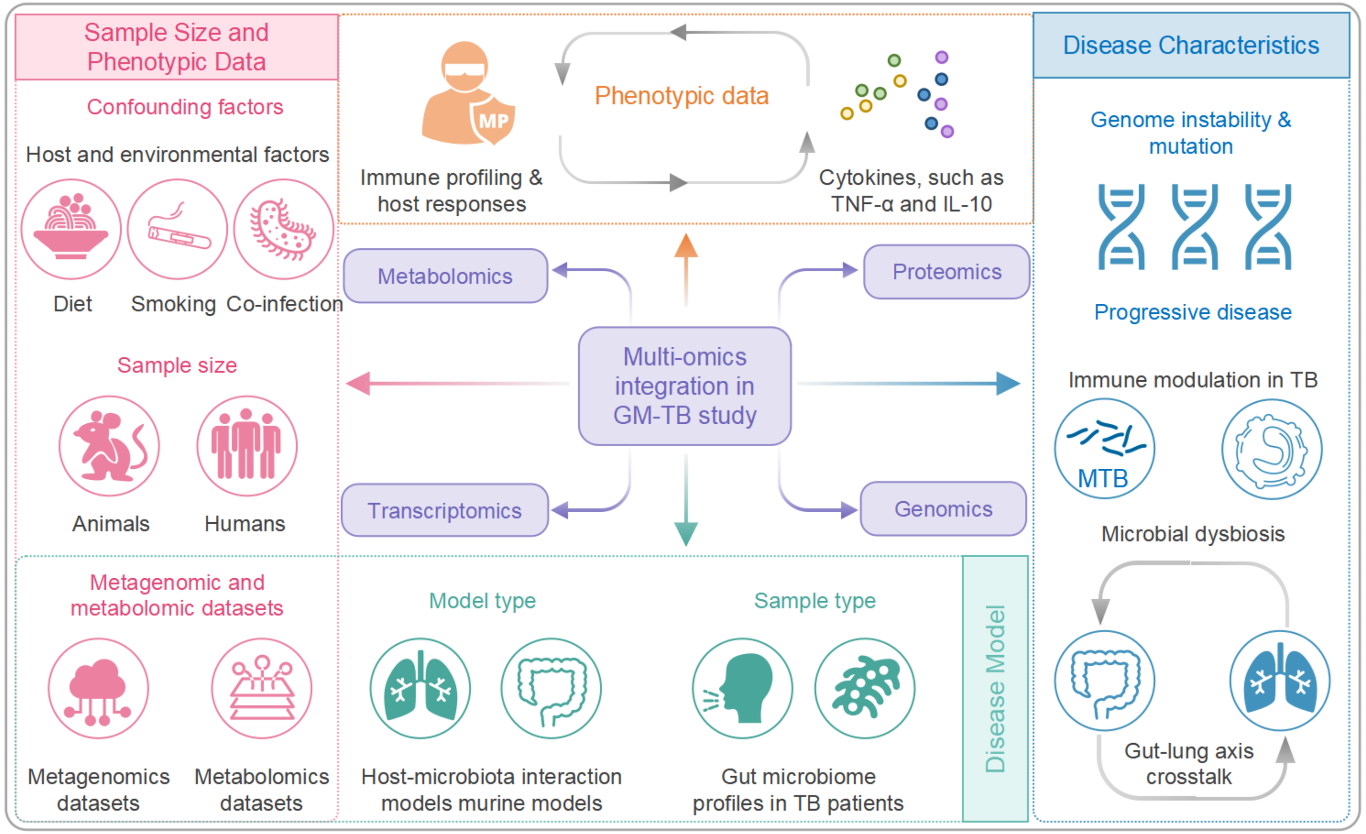


Figure 10 Applications of AI/ML in microbiome research: from data collection to implementation

Figure 11 Integrative multi-omics framework for investigating GM-TB interactions



Current Challenges and Future Directions in GM-TB Research

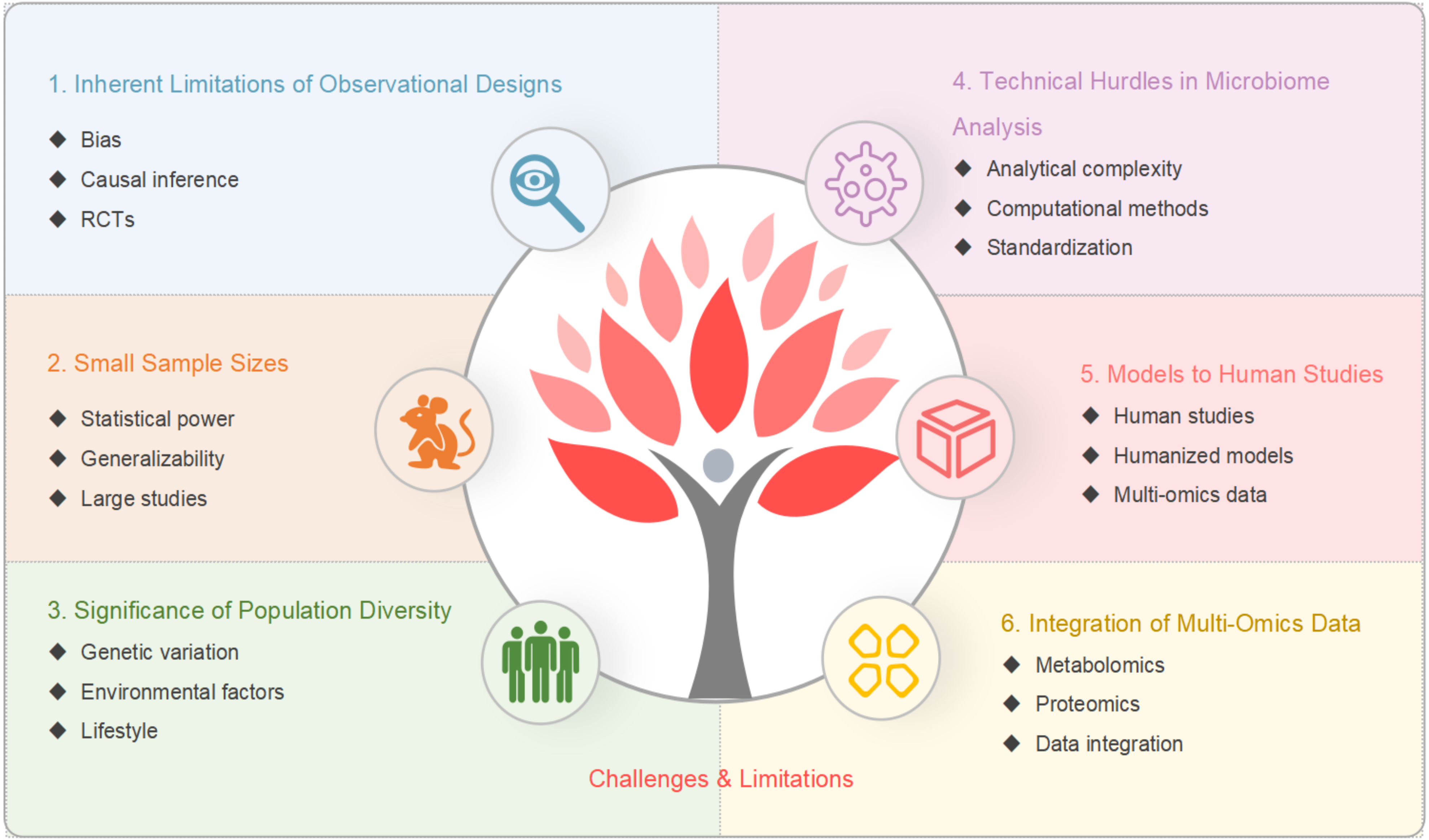


Figure 12 Challenges and Limitations in GM-TB Studies

Current Challenges and Future Directions in GM-TB Research

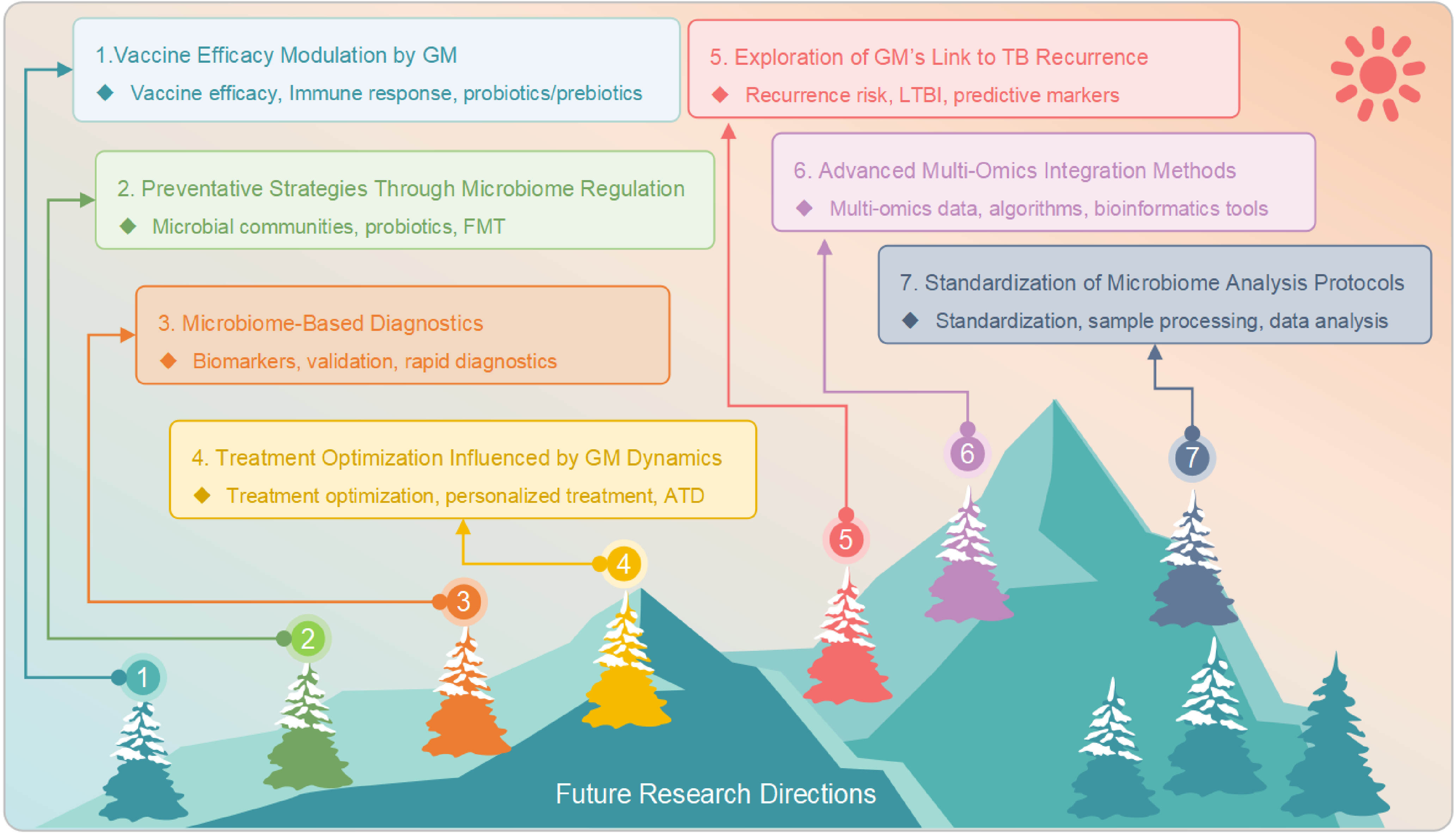


Figure 13 Future directions and research priorities in GM-TB studies

Conclusion

◆ **Gut microbiome - tuberculosis interaction pattern**

Tuberculosis patients have reduced gut microbiome diversity, altered specific taxa, and functional network imbalances linked to disease progression and prognosis.

◆ **Mechanistic insights**

The gut microbiome regulates host immunity, affects Mycobacterium tuberculosis metabolism, and is involved in drug responses, with immune modulation being central.

◆ **Translational prospects**

Microbiome - based diagnostics can improve accuracy, microbiome modulation can enhance therapeutic effects and reduce side effects, and probiotic interventions have preventive potential.

◆ **Technological frontiers and challenges**

While NGS and AI/ML technologies drive multi - omics integration and predictive model development, issues like sample heterogeneity, geographic biases, and insufficient mechanistic validation require large - scale prospective studies to accelerate clinical translation.

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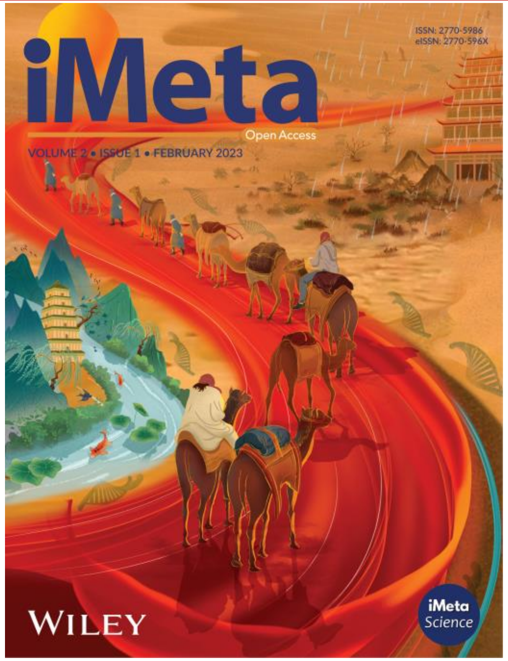

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