Microbial metabolites in tumor epigenetic regulation

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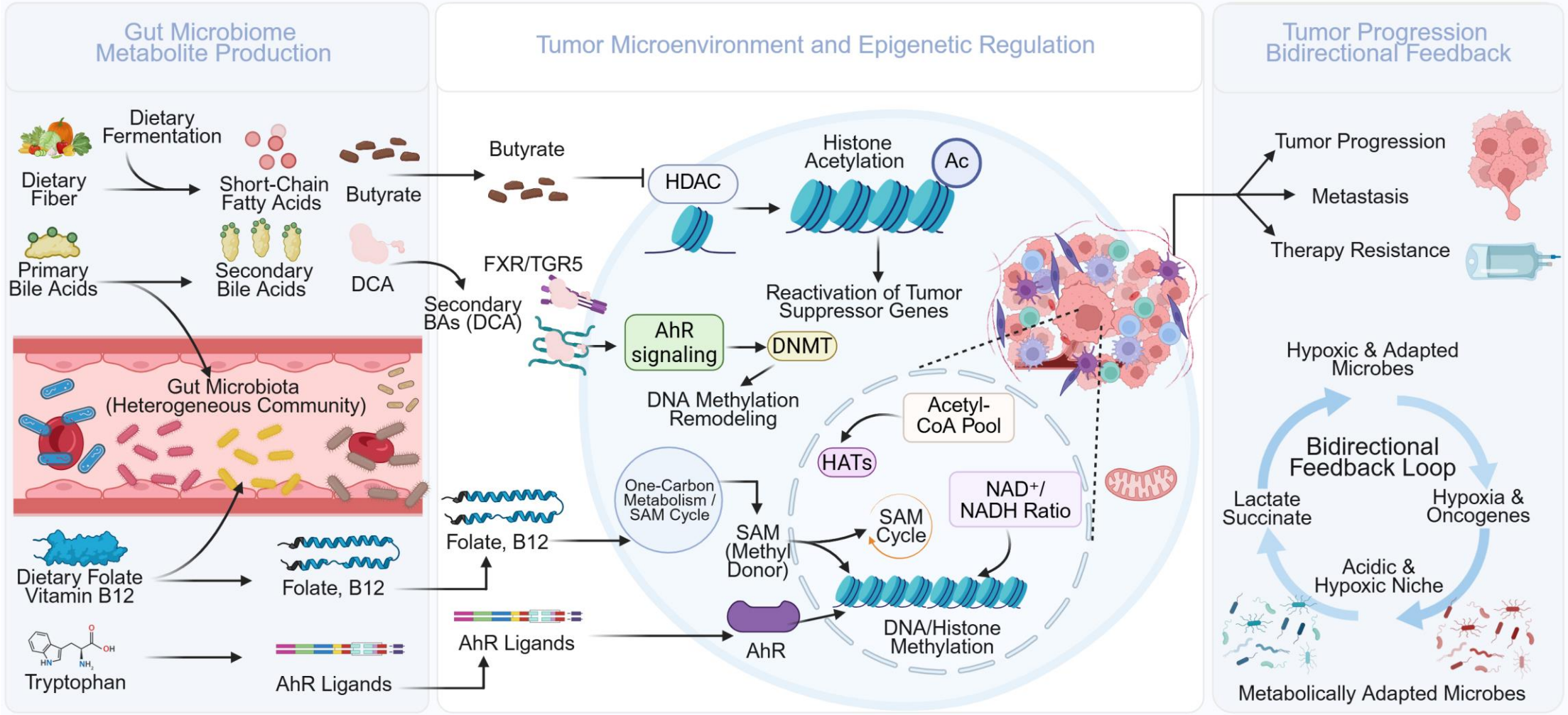
Graphical Abstract



Challenges and Precision Oncology Implications

Current Challenges

Causality - Spatiotemporal dynamics
TME heterogeneity - Dose-response

Research Strategies

Multi-omics integration, Spatial metabolomics
CRISPR biosensors

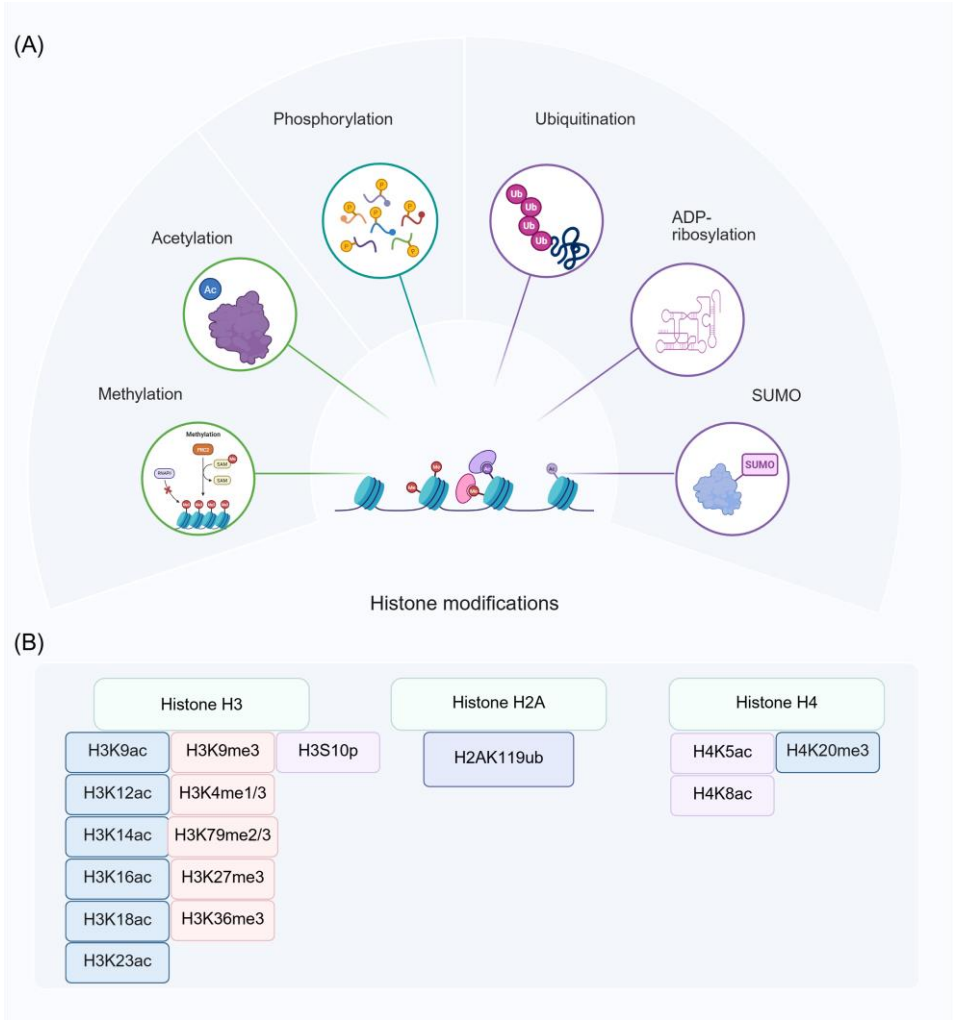
Goal: Precision Oncology

Microbiome-epigenetic axis targeting therapy
Novel biomarkers - Personalized therapy

Highlights

- Microbial metabolites, such as butyrate and bile acids, regulate tumor progression by modifying histone deacetylases and DNA methylation.
- Microbial metabolites modulate immune cell functions, influencing tumor progression and enhancing the effectiveness of immune therapies.
- Tumor-induced metabolic changes promote specific microbes, which reinforce epigenetic dysregulation, creating a bidirectional feedback loop.
- Microbial-derived vitamins and amino acids regulate DNA and histone methylation, impacting tumor suppressor genes and metabolic pathways.

Histone modifications



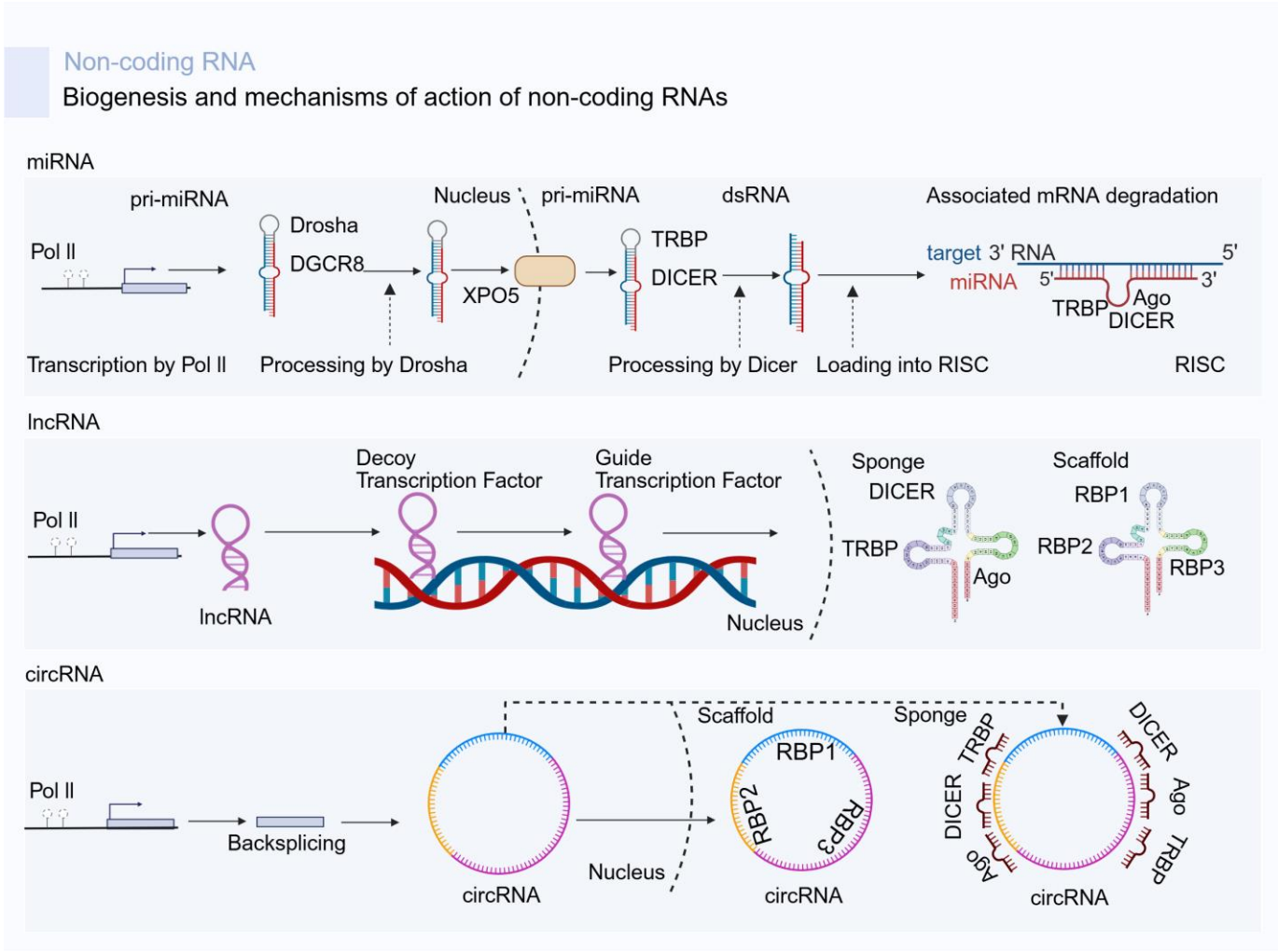


Figure 8 Overview of various PTM types and their main modification sites on different histone subunits.

Figure 9 Biogenesis of ncRNAs and their mechanisms of action.

Chromatin 3D structure remodeling

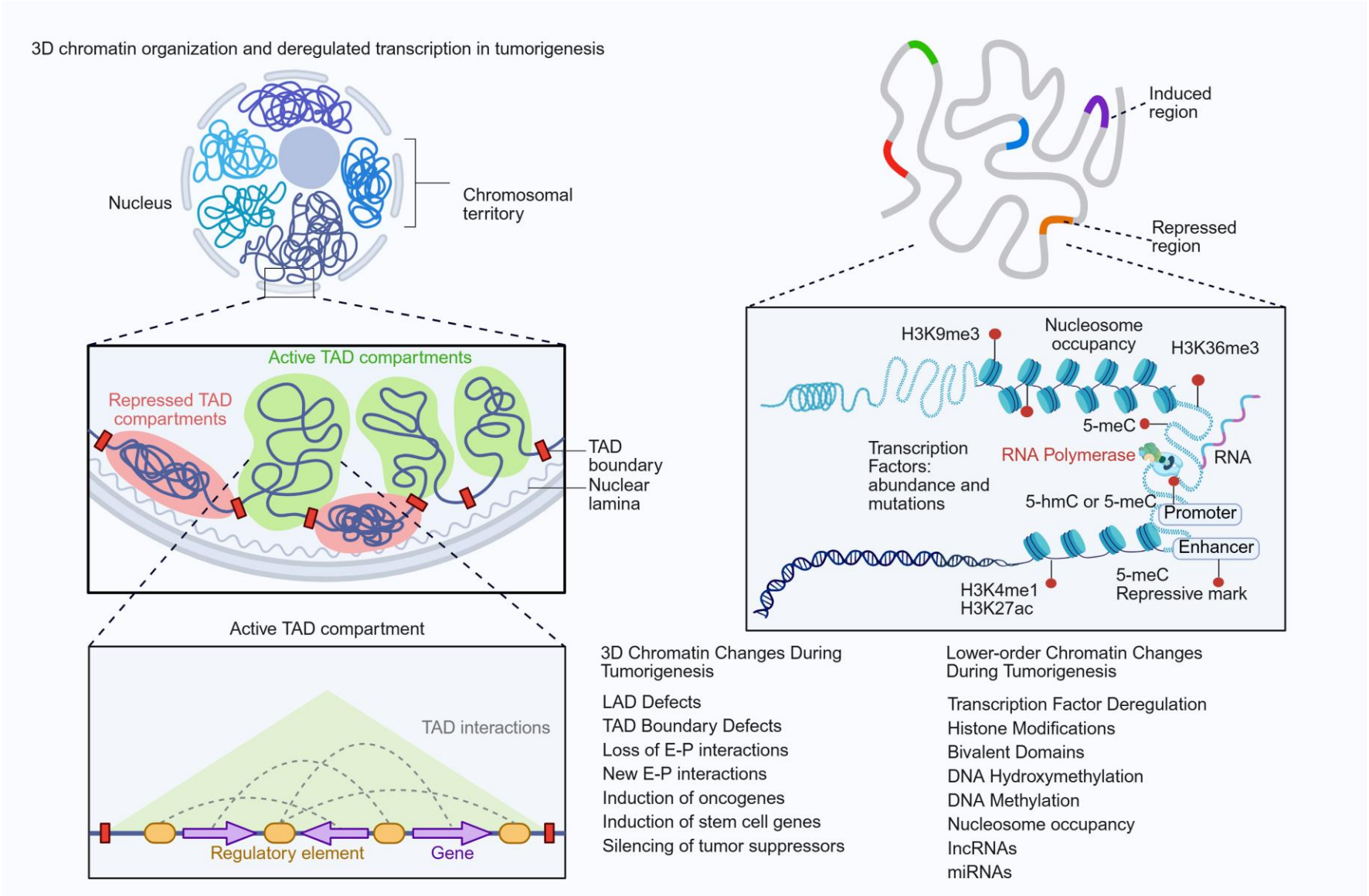


Figure 11 Three-dimensional chromatin remodeling and transcriptional dysregulation mechanisms play a crucial role during tumorigenesis.

Clinical trials and translational perspectives

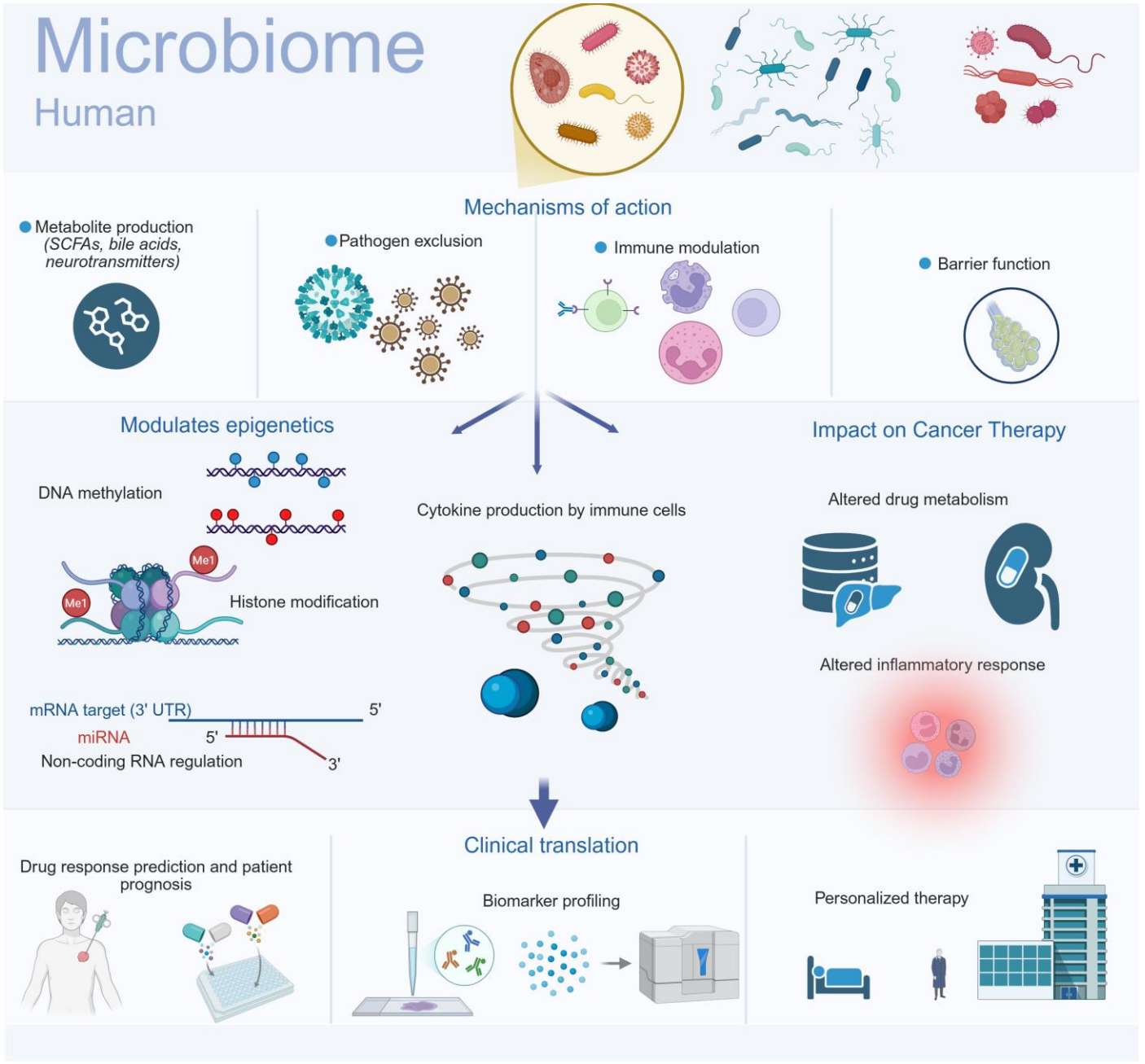


Figure 20 Multilayered mechanisms linking the human microbiome to cancer therapy and clinical translation.

Summary

- This paper systematically summarizes the core mechanisms of microbial metabolites regulating tumor epigenetics and their bidirectional feedback loop.
- Microbial metabolites (e.g., SCFAs, secondary bile acids) affect tumor progression and immunotherapy response via histone acetylation, DNA methylation and other modifications.
- Tumor metabolic reprogramming reshapes the microbiota, and microbial metabolites further intensify tumor epigenetic dysregulation, forming a pro-tumorigenic self-reinforcing cycle.
- Current research faces challenges in causal dissection, individual differences and technical integration; multi-omics and AI are needed to drive clinical translation for precision oncology.

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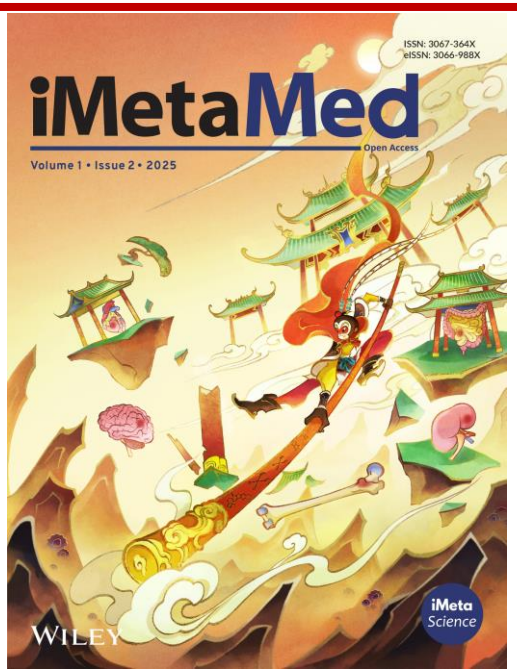

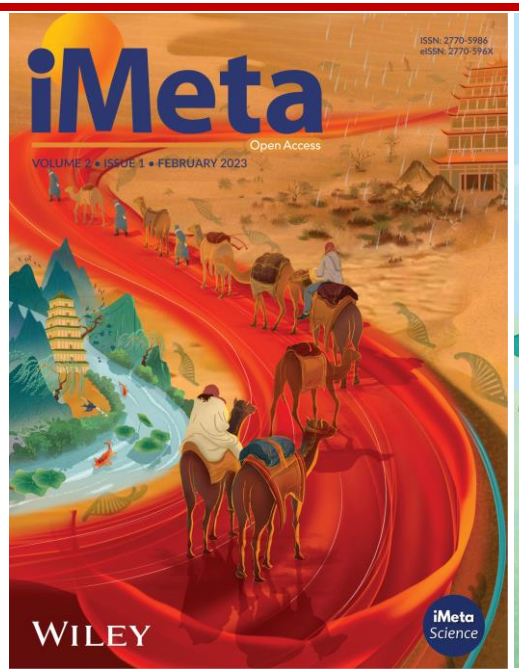

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