Microbiome-urothelium crosstalk in bladder cancer: From dysbiosis to clinical translation
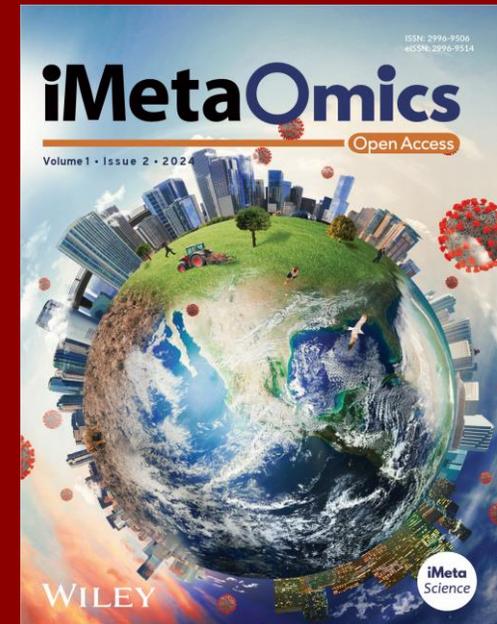
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Bladder Cancer & Urobiome

- **Paradigm Shift**: Advanced sequencing confirms the "Urobiome" exists, overturning the "sterile urine" dogma.
- **Microbial Dysbiosis**: BCa is characterized by pathogen enrichment and beneficial bacteria depletion.
- **Tumorigenesis**: Driven by chronic inflammation, bacterial genotoxins, and metabolic reprogramming.

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Clinical Challenges & Translation

- **Current Limitations**: Invasive diagnostics (cystoscopy) and variable treatment responses (BCG/ICIs).
- **Liquid Biopsy**: Urobiome serves as a non-invasive biomarker for diagnosis and risk stratification.
- **Precision Intervention**: Enables response prediction and novel therapies like probiotics and FMT.

Core Contributions

Systematically integrating urobiomics with clinical translation. We map the path from dysbiosis and mechanisms to precision medicine, highlighting the microbiome's role in diagnosis, prognosis, and therapeutic modulation.

Highlights
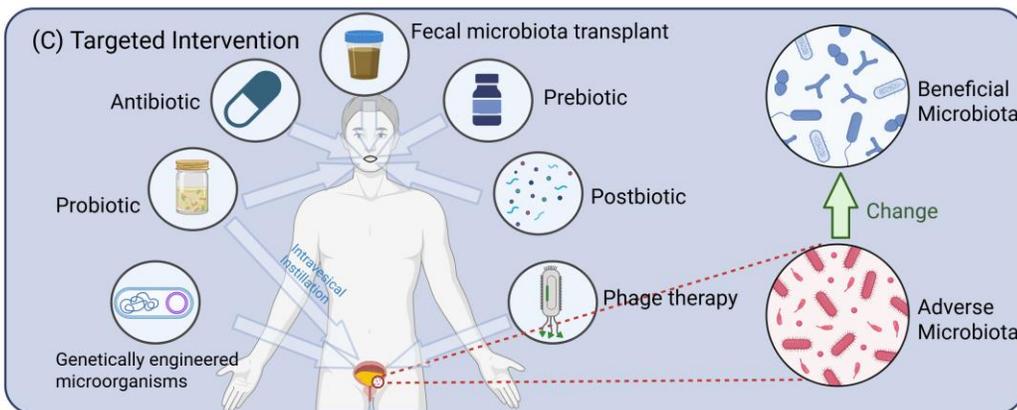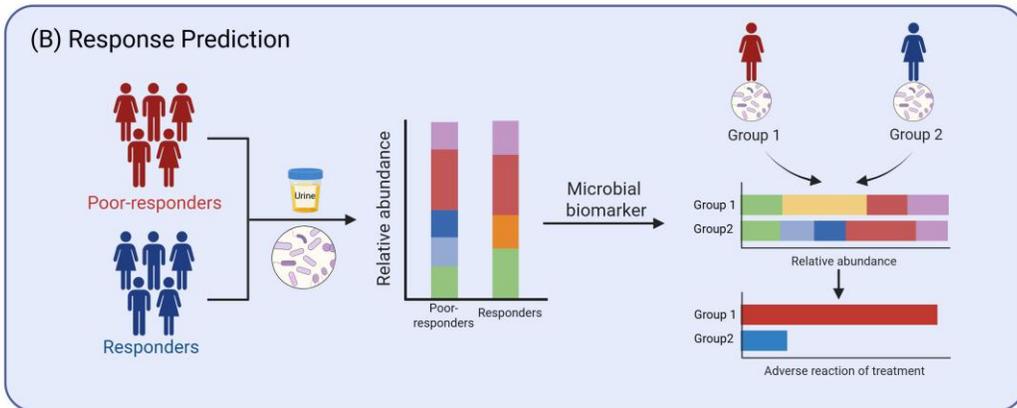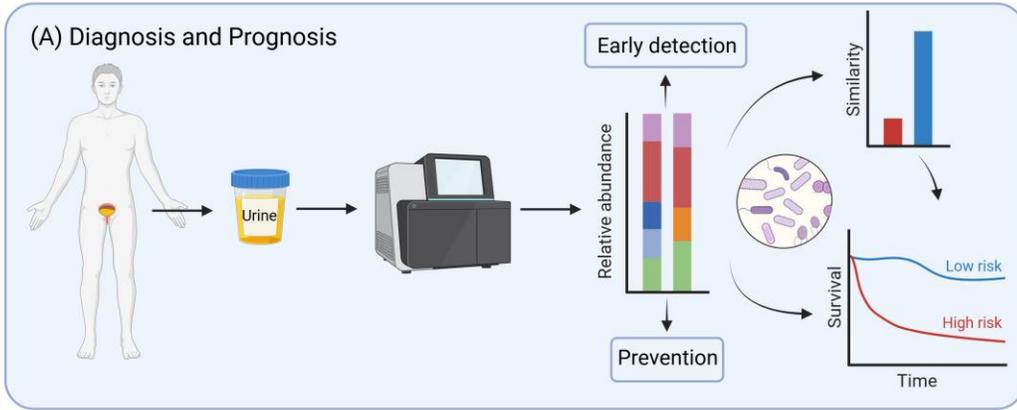
☑ The urinary microbiome exhibits distinct dysbiosis in bladder cancer, providing specific microbial signatures for non-invasive diagnosis and risk stratification.

☑ Mechanistic crosstalk drives tumorigenesis through chronic inflammation, bacterial genotoxins, and metabolic reprogramming via the gut-bladder axis.

☑ Microbial profiles serve as robust predictors of therapeutic efficacy for both intravesical BCG immunotherapy and systemic ICIs.

☑ Personalized strategies, including microbiome-conscious antibiotic stewardship and probiotic interventions, offer novel avenues to enhance bladder cancer treatment outcomes.

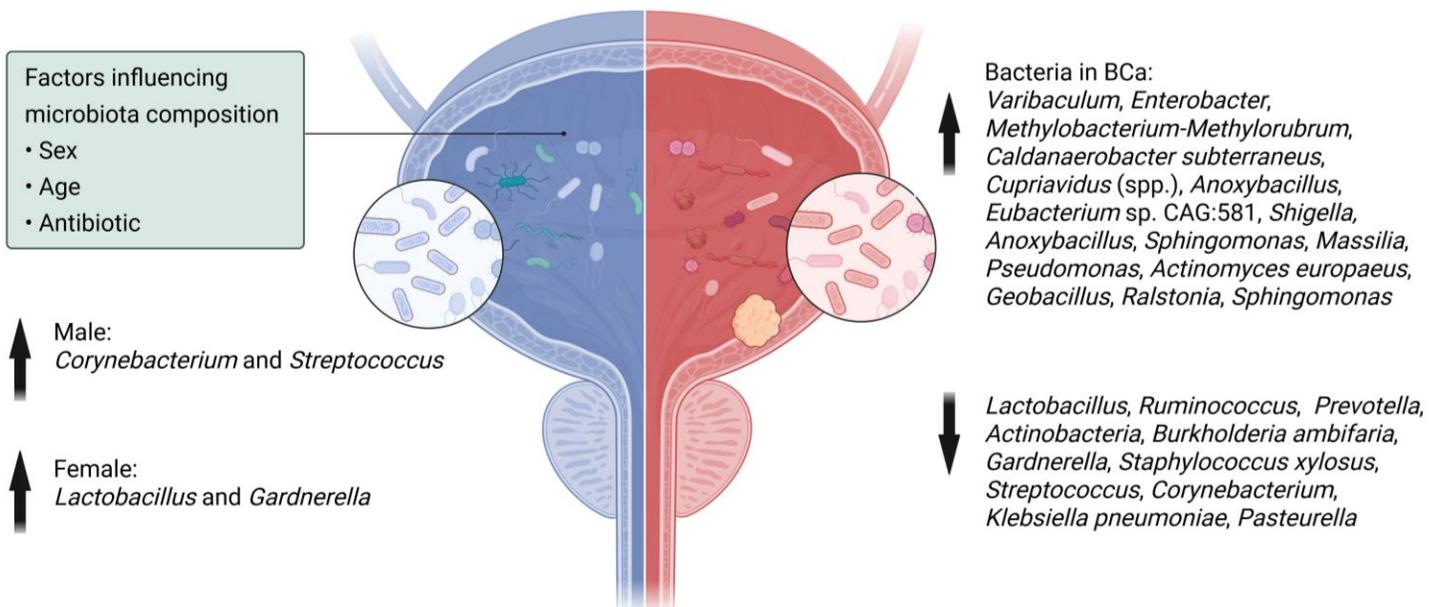Figure 1 Comparison of the urinary microbiome in health versus cancer and implications of sampling methodologies.

Sampling Method Evaluation
- Midstream Urine (CC): High contamination risk; reflects "urogenital" microbiota.
- Catheterized (TUC) / Suprapubic (SPA): Accurately reflects the "bladder" niche; ideal for cancer research.

Homeostasis
- Females: Dominated by Lactobacillus.
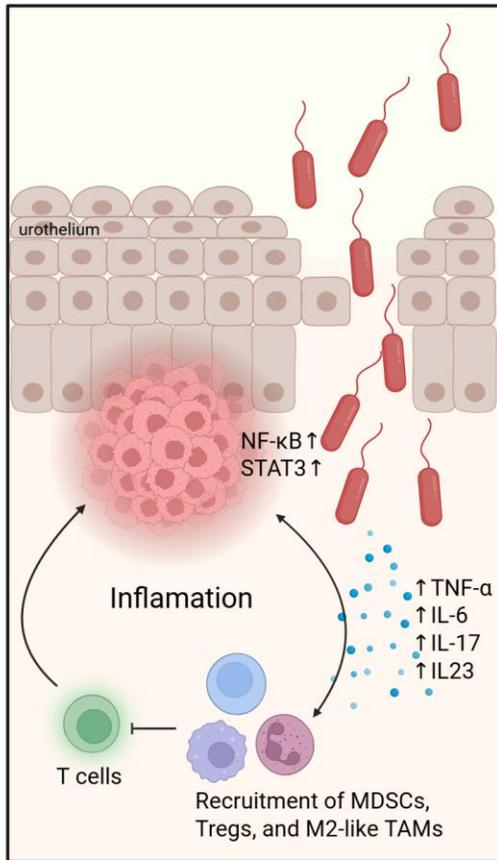- Males: Dominated by Corynebacterium & Streptococcus.

Dysbiosis in BCa
- Enriched: Potential pathogens (e.g., Enterobacter, Streptococcus).
- Depleted: Beneficial commensals (e.g., Lactobacillus, Bifidobacterium).

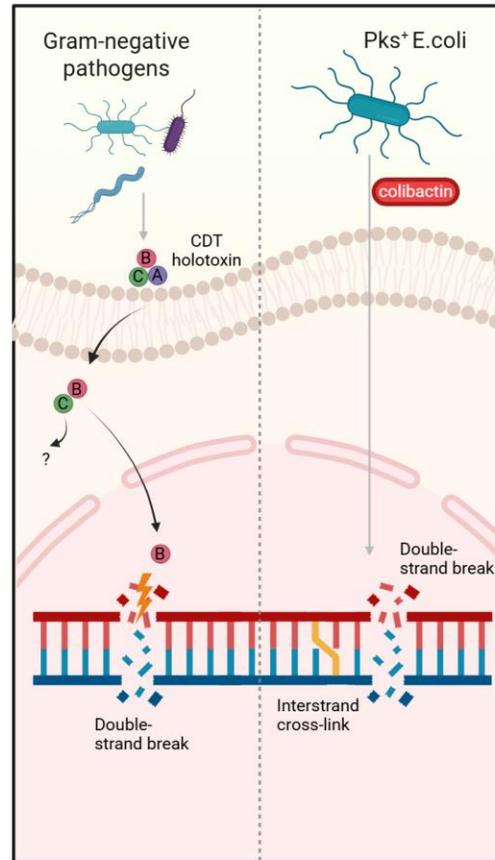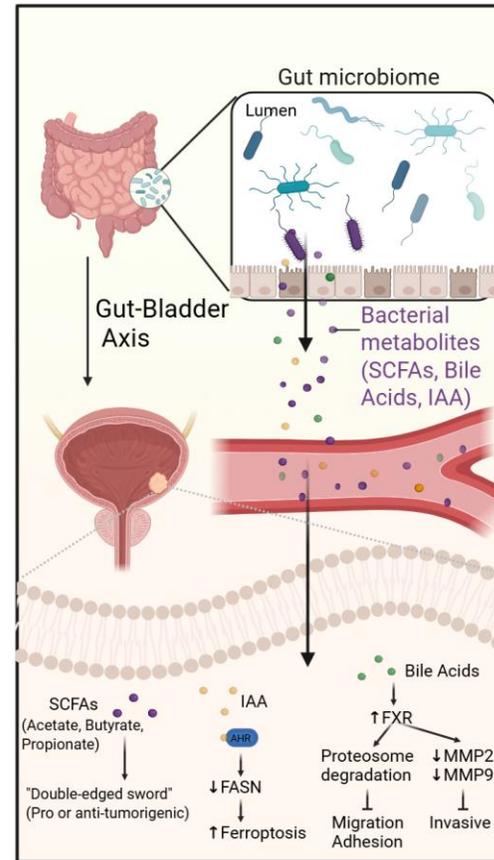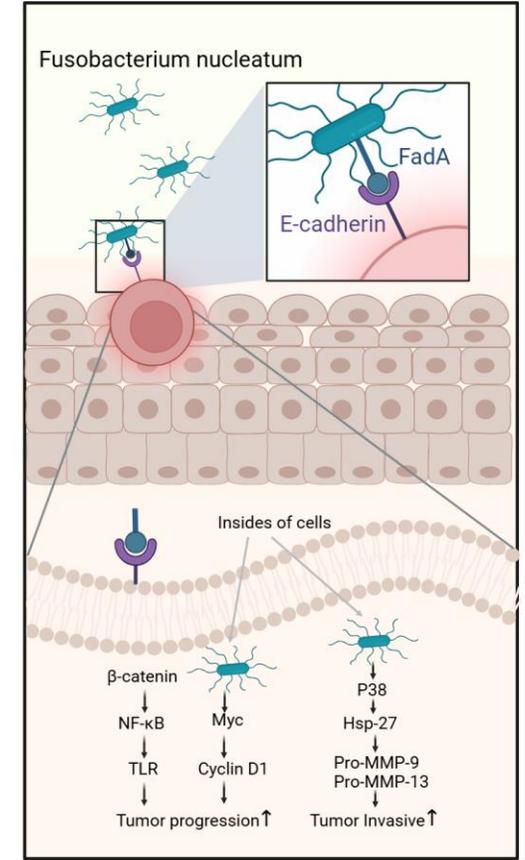Figure 2 Putative mechanisms by which the microbiome promotes bladder carcinogenesis.
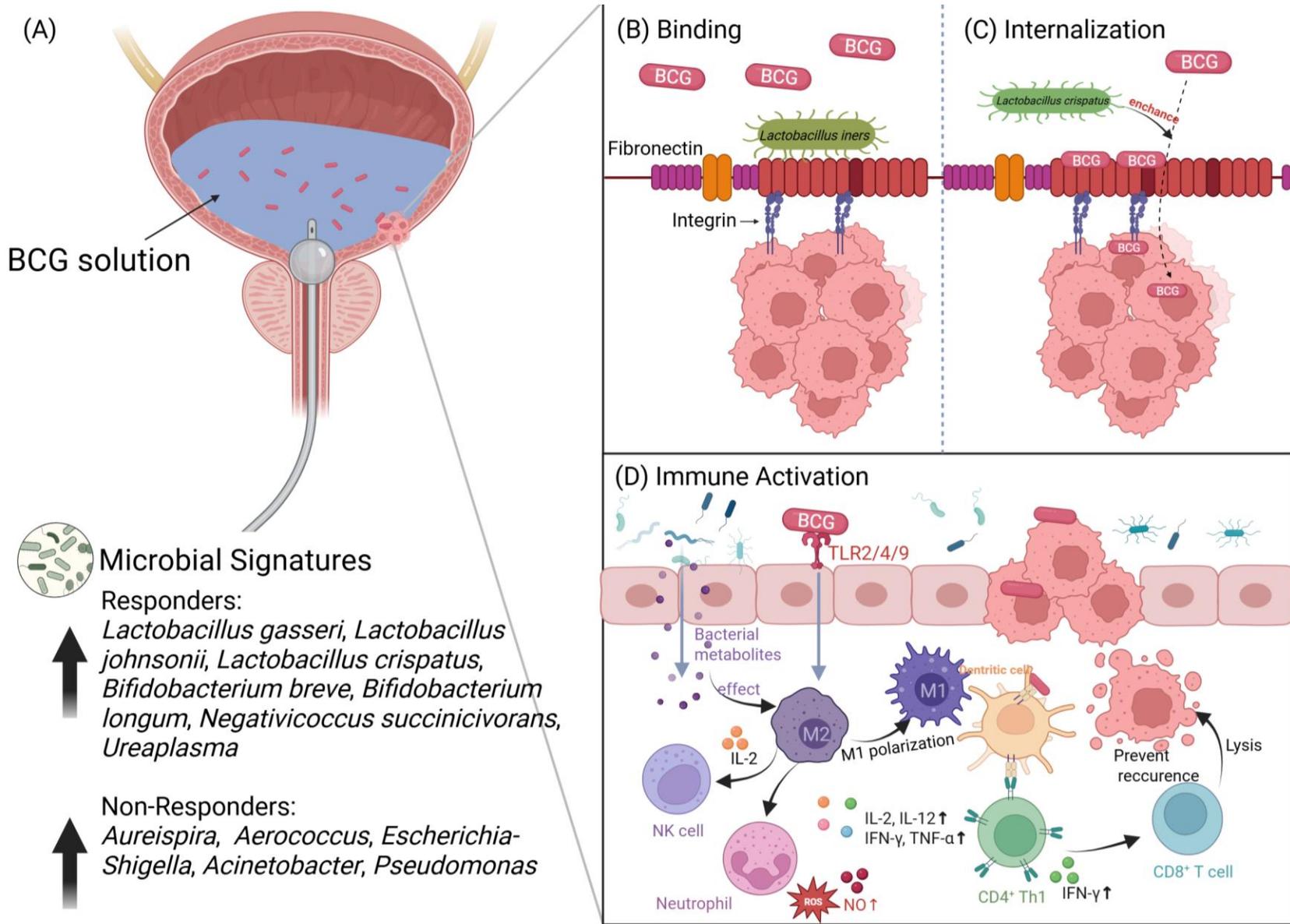
Figure 3 Proposed mechanisms modulating BCG immunotherapy efficacy via the urinary microbiome.

Figure 4 Clinical applications of the microbiome in bladder cancer management.
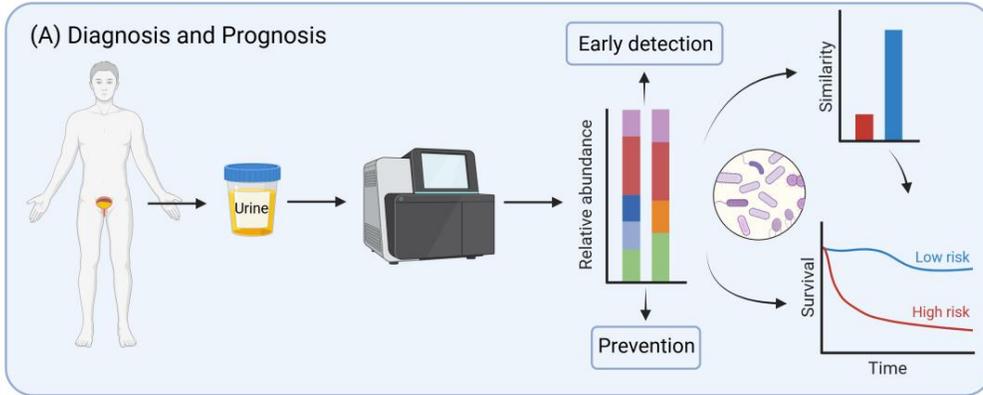
Diagnosis & Prognosis (Liquid Biopsy)
➢ Early Detection: Utilization of the urinary microbiome as non-invasive biomarkers.
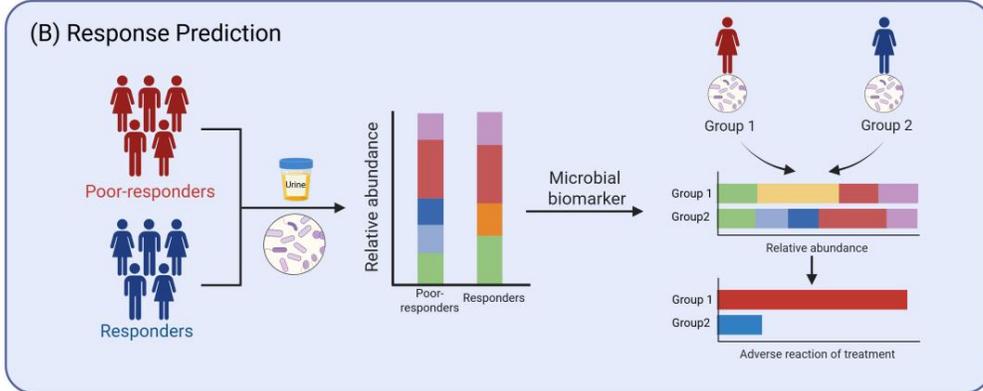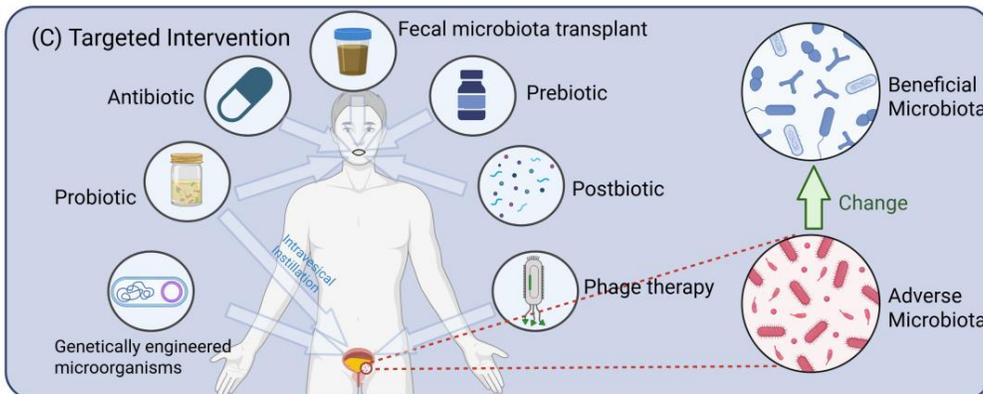➢ Risk Stratification: Distinguishes high-risk vs. low-risk groups to predict survival outcomes.

Response Prediction
➢ Signature Identification: Pre-treatment differentiation of Responders vs. Non-Responders.
➢ Precision Selection: Screens potential beneficiaries to maximize immunotherapy efficacy and minimize adverse events.

Targeted Intervention (Microbiome Reshaping)
➢ Goal: Reverses pro-tumor dysbiosis into a beneficial state.
➢ Strategies: Probiotics, FMT (Fecal Microbiota Transplant), prebiotics, postbiotics, and phage therapy.

Summary & Perspectives

○ Dysbiosis Landscape: Constructed a bladder cancer-specific microbial map, integrating microbiomics with clinical translation beyond the "sterile urine" dogma.

○ Mechanistic Insights: Elucidated host-microbe crosstalk driving tumorigenesis via chronic inflammation, bacterial genotoxicity, and the gut-bladder metabolic axis.

○ Clinical Utility (Liquid Biopsy): Established the microbiome as a non-invasive tool for early diagnosis, risk stratification, and predicting immunotherapy response (BCG/ICIs).

○ Methodological Standardization: Addressed challenges in low-biomass samples by proposing standardized sampling and contamination control workflows.

○ Precision Intervention: Proposed a shift from "observation" to "action," targeting the microbiome (e.g., probiotics, FMT) for personalized precision oncology.
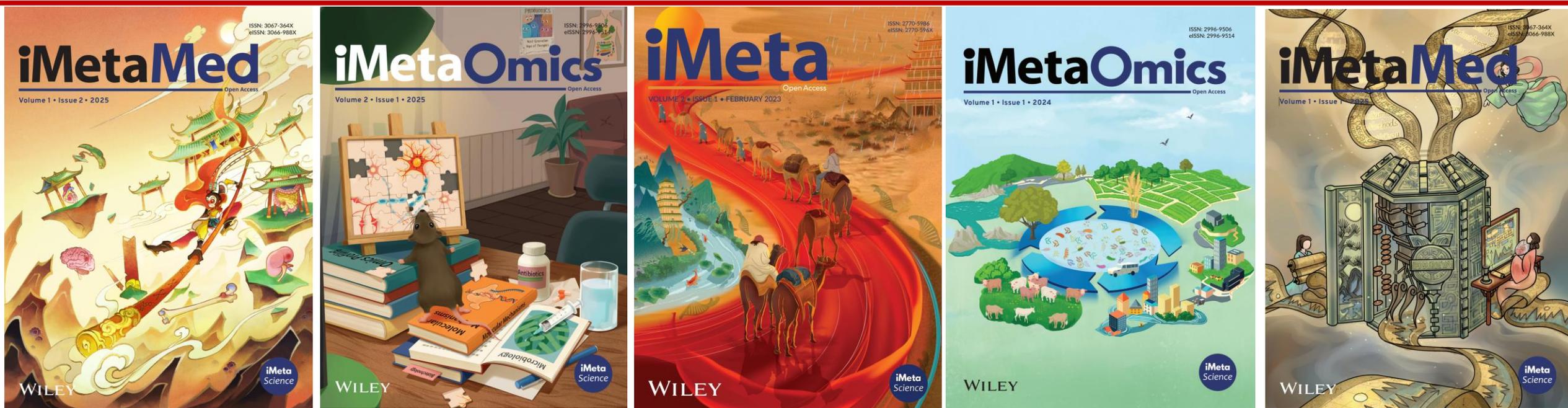
iMeta: To be top journals in biology and medicine

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"*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.