

Gut Microbiome Therapeutics for Colorectal Cancer: Advances in Bacteria and Phage Driven Interventions

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Abstract

Colorectal Cancer (CRC) remains a major global health burden, with over 1.9 million new cases reported in 2022 and a rising incidence worldwide. Although advances in surgery, chemotherapy, and immunotherapy have improved outcomes, their effectiveness is often limited by drug resistance, immune evasion, and treatment-associated toxicity. Recent research has shifted focus toward the gut microbiome as a critical regulator of colorectal carcinogenesis and therapeutic response. Microbial dysbiosis actively contributes to CRC progression through genotoxic metabolite production, chronic inflammation, and immune modulation.

Oncogenic species such as *Fusobacterium nucleatum*, enterotoxigenic *Bacteroides fragilis*, and pks⁺ *Escherichia coli* play key roles in establishing a pro-tumorigenic microenvironment. In parallel, the gut phageome has emerged as an important determinant of microbial dynamics, with disease-associated signatures offering both diagnostic and therapeutic potential. This review evaluates two rapidly advancing therapeutic strategies, including microbiome-restorative approaches such as fecal microbiota transplantation, engineered probiotics, and live biotherapeutic products, and bacteriophage-based interventions that enable strain-specific targeting of oncogenic bacteria while preserving beneficial commensals. Notably, combinatorial strategies integrating both modalities demonstrate enhanced efficacy in preclinical models. Using a PRISMA-guided framework, this review synthesizes mechanistic, preclinical, and early clinical evidence to outline a roadmap for microbiome-based CRC therapeutics and their potential to advance precision oncology.

Index Terms

Colorectal Cancer; Gut Microbiome; Bacteriophage Therapy; Fecal Microbiota Transplantation; Dysbiosis; Tumor Microenvironment; Precision Oncology; Phageome; Live Biotherapeutic Products