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Policy Brief:

The Role of Gut Microbiota in Colorectal Cancer Management: A New Strategy in Health Policymaking

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Abstract

Background and Objective: Colorectal cancer remains a leading cause of cancer-related mortality, driven largely by the complex interplay between host genetics and the gut microbiota. The objective of this study is to develop evidence-based health policy recommendations for integrating microbiome profiling into national CRC screening and management protocols.

Material and Methods: Evidence from major databases and an approved project on CRC microbiota was synthesized through translational policy analysis to map biological mechanisms against clinical guidelines and identify strategic gaps.

Results and Conclusion: A robust, multidimensional policy framework is urgently needed to bridge the translational gap between microbiome research and clinical oncology. We propose specific policy recommendations to establish standardized microbial profiling in routine CRC screening, fund longitudinal studies on host-microbe interactions, and integrate bioinformatic tools into clinical decision-making. These strategic shifts will enable the transition from reactive treatment to proactive, microbiome-informed precision care, ultimately reducing CRC mortality and healthcare burdens.

Keywords: Colorectal Cancer, Gut Microbiota, Health Policy

1. Introduction and statement of the problem

Colorectal cancer (CRC) remains a leading cause of cancer-related mortality worldwide, imposing a profound and escalating burden on global healthcare systems. While conventional oncological paradigms have historically prioritized host genetics as the primary driver of carcinogenesis, recent research has shifted focus toward the critical influence of the gut microbiota in human health and disease [1].

As a dynamic and complex “virtual organ,” the gut microbiota is integral not only to physiological processes—such as nutrient metabolism and digestion—but also to the modulation of inflammatory pathways through the production of bioactive metabolites and continuous cross-talk with the host immune system [2]. Mounting evidence suggests that microbial imbalance, or dysbiosis, serves as a

The clinical management of colorectal cancer (CRC) is fundamentally challenged by its complex, multifactorial etiology. CRC is not merely a consequence of intrinsic genetic aberrations; rather, it emerges from a deleterious interplay between environmental exposures and the gut microbial ecosystem [1]. Mounting evidence indicates that shifts in the composition of the gut microbiome exert a direct regulatory influence on cellular signaling pathways and the expression of genes involved in apoptosis and cell proliferation [2].

Experimental evidence supports this: *in vitro* studies employing the MTT assay on HT29 cell lines have demonstrated that metabolites derived from the microbiota of CRC patients significantly modulate cancer cell viability, highlighting the direct impact of microbial products on tumor phenotype [3]. Furthermore, therapeutic resistance has emerged as a significant barrier to successful clinical outcomes. Recent data suggest that the gut microbiota plays a pivotal role in modulating the host’s response to both conventional chemotherapy and emerging immunotherapies [4]. Consequently, the current clinical landscape suffers

from a critical deficiency: the absence of precise, non-invasive risk assessment tools and validated diagnostic signatures based on microbial profiles. Addressing this gap is essential for the evolution of more effective, personalized screening and therapeutic protocols.

2. Methods

We conducted a targeted search of peer-reviewed literature and clinical guidelines across PubMed/MEDLINE, Scopus, and Web of Science, supplemented by hand-searching key references and finding was supported further informed by materials derived from the approved project "Alterations in the gut microbiota and their metabolites in human intestinal epithelial cells of patients with colorectal cancer". This evidence was synthesized using a translational policy analysis approach to map biological mechanisms against existing clinical guidelines and identify gaps for strategic directives

3. Results

Systems biology analyses reveal that colorectal cancer (CRC) originates from a dysregulated network of genes and proteins, significantly modulated by the gut microbial ecosystem [2]. Under conditions of microbial homeostasis, specific metabolites—most notably short-chain fatty acids (SCFAs)—exert potent anti-tumorigenic effects. Conversely, the onset of dysbiosis precipitates a decline in these protective metabolites coupled with an upregulation of pro-inflammatory compounds. This biochemical shift compromises the integrity of the intestinal mucosal barrier, thereby fostering a microenvironment conducive to neoplastic transformation and tumor progression [4-6].

Concurrently, innovative therapeutic modalities are currently exploring the "manipulation" of the microbiome to reverse treatment resistance and restore cancer cell sensitivity to chemotherapy and immunotherapy [4]. Given the multifaceted nature of these host-microbe interactions, the integration of bioinformatic data analysis with longitudinal microbial profiling offers a promising roadmap for the next generation of precision therapies. As current research underscores, elucidating the precise molecular mechanisms that govern this cross-talk is critical for identifying novel therapeutic targets and systematically mitigating the prevalence of resistance to oncological interventions [4].

4. Health Policy Framework

Translating foundational laboratory insights into actionable clinical practice necessitates the development of a robust and multidimensional policy framework. To bridge this translational gap, a comprehensive strategy must be established, centered upon four fundamental pillars:

1. Standardization and Regulatory Oversight

The integration of emerging therapies, such as fecal microbiota transplantation (FMT) and the utilization of genetically engineered bacterial strains, requires the establishment of stringent ethical and regulatory frameworks. To ensure patient safety and therapeutic consistency, it is imperative to develop standardized protocols for the sourcing, processing, and clinical application of these microbial interventions. Such regulatory oversight is essential to mitigate potential risks and provide a secure, evidence-based foundation for their adoption in routine clinical practice.

2. Microbial Screening and Diagnostic Integration:

Health policymakers should prioritize the development and validation of "microbial signature" assays as diagnostic adjuncts within national screening programs. By leveraging high-resolution microbiome data, these non-invasive diagnostic tools offer a transformative approach to early risk stratification. The widespread implementation of such screening strategies would significantly enhance the early detection of colorectal cancer, enable timely clinical intervention and improve long-term prognostic outcomes for high-risk populations.

3. Equitable Distribution of Nutritional Interventions: Public health initiatives should systematically promote, as a cost-effective and evidence-based strategy, lifestyle modifications that foster gut microbiome homeostasis—such as the adoption of high-fiber diets and the regular consumption of fermented foods. Integrating these nutritional paradigms into national noncommunicable disease (NCD) prevention programs represents a high-impact, scalable strategy to improve population-level gut health. By institutionalizing these preventative measures, policymakers can effectively reduce the burden of chronic intestinal inflammation, thereby decreasing the long-term incidence of colorectal malignancy.

4. Precision and Personalized Therapeutics

Policymakers must champion interdisciplinary research initiatives that aim to correlate individual microbial profiles with standard oncological treatment protocols. By transitioning toward a model of precision medicine, clinicians can tailor therapeutic strategies to the unique microbial landscape of the patient, thereby minimizing adverse events and maximizing therapeutic efficacy. This personalized approach not only optimizes clinical outcomes but also addresses the challenge of treatment resistance, marking a paradigm shift in the standard of care for colorectal cancer.

5. CONVERT TO POLICY

In the contemporary medical landscape, colorectal cancer (CRC) has emerged as an exceptionally complex malignancy that cannot be effectively managed without accounting for the multifaceted role of the gut microbiota—the patient's "virtual organ." Empirical evidence consistently demonstrates that the intestinal microbiota acts as a primary determinant not only in the pathophysiology of CRC but also in influencing clinical outcomes and therapeutic responsiveness.

Integrating comprehensive "microbial risk assessment" into national screening protocols and incorporating "microbial modulators" into standard therapeutic regimens offer the potential to fundamentally transform patient survival rates and long-term quality of life. Health policymakers should evaluate the formal adoption of microbiome-based interventions as a robust third arm of cancer care, operating in synergy with traditional surgical and chemotherapeutic modalities. The future of CRC management lies in the convergence of systems biology, precision diagnostics, and intelligent microbial engineering. Achieving this clinical transition requires a prioritized, sustained investment in interdisciplinary research, bridging the gap between bench-side discovery and bedside application to redefine the standard of care.

6. Declarations

6.1. Acknowledgement

Ethics approval and consent to participate

This study was supported financially by a grant [no. RIGLD 1090, IR.SBMU.RIGLD.REC.1399.011] from Foodborne and Waterborne Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

6.2. Conflict of Interest

All authors declare no conflict of interest.

6.3. Using chatbots

AI language model was used for language editing and proofreading

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خلاصه سیاستی:

نقش میکروبیوتای روده در مدیریت سرطان کولورکتال: راهبردی نوین در سیاست‌گذاری سلامت

سمیه جهانی‌شرافت

مرکز تحقیقات کاربرد لیزر در علوم پزشکی، دانشگاه علوم پزشکی شهید بهشتی، تهران، ایران

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چکیده

سابقه و هدف: سرطان روده بزرگ یکی از علل اصلی مرگ‌ومیر ناشی از سرطان است که ناشی در تعامل پیچیده بین ژنتیک میزبان و میکروبیوتای روده دارد. هدف این مطالعه، سیاستگذاری در سلامت مبتنی بر شواهد برای یکپارچه‌سازی بررسی میکروبیوم در پروتکل‌های ملی غربالگری و مدیریت سرطان روده بزرگ است.

مواد و روش ها: نتایج به دست آمده از پایگاه‌های داده معتبر و یک پروژه مصوب در زمینه میکروبیوتای CRC، بررسی شدند تا مکانیسم‌های زیستی با راهنماهای بالینی تطبیق داده شده و شکاف‌های راهبردی شناسایی گردند.

یافته‌ها و نتیجه‌گیری: نیاز فوری به یک چارچوب سیاستی قدرتمند و چندبُعدی برای پر کردن شکاف بین تحقیقات میکروبیوم و آنکولوژی بالینی وجود دارد. ما پیشنهادهای سیاستی مشخصی را برای ایجاد پروفایل‌نگاری استاندارد میکروبی در غربالگری‌های روتین CRC، تأمین مالی مطالعات درباره تعامل میزبان و میکروب، و ادغام ابزارهای بیوانفورماتیکی در تصمیم‌گیری بالینی ارائه دادیم. این تغییرات راهبردی امکان گذر از درمان به پیشگیری مبتنی بر میکروبیوم را فراهم کرده و در نهایت مرگ‌ومیر و بار اقتصادی ناشی از سرطان روده بزرگ را کاهش خواهد داد.

واژگان کلیدی: سرطان روده بزرگ، میکروبیوتای روده، سیاستگذاری سلامت