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EDITORIAL

Gut microbiome: an emerging player and therapeutic target in cancer

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The human gut microbiome plays critical roles in cancer. These gut microorganisms and their derivatives influence nearly every aspect of the disease, including tumor development and progression to metastasis, as well as therapeutic efficacy. Given this importance, emerging research is focusing on novel strategies aimed at targeting the gut microbiome to improve patient outcomes. This special issue brings together a collection of Reviews, Letter, and Research Articles exploring the multifaceted roles of the microbiome, providing functional and mechanistic insights, and discussing the clinical potential of current microbiome-targeting strategies.

This special issue begins with seven Reviews focusing on the roles of the gut microbiome in various aspects of cancer. One review elucidates how the gut microbiome and its derived metabolites shape the immunotherapy response in hepatocellular carcinoma, and explores microbiome-targeting strategies for enhancing treatment outcomes. The second review describes the antitumor mechanisms of probiotics in suppressing colorectal cancer (CRC) and describes combining probiotics with standard regimens to overcome therapeutic resistance. One review summarizes current research on the intratumoral microbiome in gastrointestinal cancers, and explains how tumor-resident bacteria interact with host tumor cells and antitumor immunity. Because immunogenic cell death is crucial for effective cancer immunotherapy, another review focuses on the microbial regulation of immunogenic cell death, and explores interventions that leverage the gut microbiome and metabolites to induce an antitumor immune response.

Emerging evidence indicates crucial roles of gut microorganisms including bacteria and fungi in pancreatic cancer. Consequently, one review explores the complete gut microbiome landscape in pancreatic cancer, including the gut microbiome's alterations and functions in pancreatic tumourigenesis, and its clinical applications as biomarkers and therapeutic targets. Beyond functional studies, animal models and analytical pipelines are critical in cancer microbiome research. One review therefore summarizes the benefits and drawbacks of various animal models of gastric cancer, and compares approaches for modeling gastric cancer progression from premalignant stages to malignancy and metastasis. Finally, a review elucidates host-microorganism interactions across the genetic, epigenomic, transcriptomic, and metabolomic landscapes. The review also introduces the current computational

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methods for integrative microbiome multi-omics analysis and their limitations.

One letter studies the effects of antibiotics and probiotics on immunotherapy outcomes in non-small cell lung cancer. Through multi-cohort meta-analysis, it reveals that antibiotics have detrimental effects on immunotherapy, whereas probiotic supplementation consistently improves treatment outcomes. These findings highlight the need for careful consideration of antibiotic use in patients, and they provide a timely rationale for the incorporation of adjuvant probiotics into cancer immunotherapy.

Four Research Articles are presented, covering both the pathogenic and protective functions of the gut microbiome in cancer. One article demonstrates that dietary nitrate significantly promotes gastritis by inducing gastric microbial dysbiosis and metabolomic dysregulation. The findings indicate that dietary intake of nitrate should be decreased or avoided for gastritis prevention and management. Another article investigates the heterogeneity in the mucosal microbiome between left-sided and right-sided CRC, and characterizes key bacterial species at multiple CRC tumor locations. This study highlights the microbial differences between left-sided and right-sided CRC, thus at least partly explaining the marked differences in the tumor microenvironment between these tumor locations.

In contrast, another article illustrates the antitumor effects of *Bifidobacterium animalis*. This probiotic bacterium not only inhibits melanoma development but also activates antitumor immunity. By combining probiotics with immune checkpoint inhibitors, this study demonstrates the potential of *B. animalis* as a robust adjuvant to enhance the immunotherapy response in melanoma. Finally, an original article evaluating the effects of SARS-CoV-2 infection on brain tumors reveals that SARS-CoV-2 infection activates the innate complement cascade with elevated intratumoral infiltration of macrophages and CD8+ T cells. These findings provide insights into the interaction between viral infection and the tumor microenvironment in brain cancer.

In summary, the diverse studies and reviews in this special issue underscore the extensive effects of the gut microbiome across multiple cancer landscapes. Although translating basic findings into clinical practice remains challenging, it is a fundamental direction for future microbiome research. We hope that the evidence and insights presented in this collection will inspire further mechanistic and clinical investigations into the complex role of the gut microbiome in cancer, and ultimately facilitate bench-to-bedside translation to improve patient outcomes.

We extend our sincere gratitude to all authors and reviewers for contributing their invaluable expertise. We are also deeply thankful to the editorial board members of *Cancer Biology & Medicine*, whose unwavering support was essential in producing this timely special issue.

Conflict of interest statement

No potential conflicts of interest are disclosed.

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