Microbiome-Driven Immunomodulation in Cancer: From Gut Bacteria to Personalized Immunotherapy

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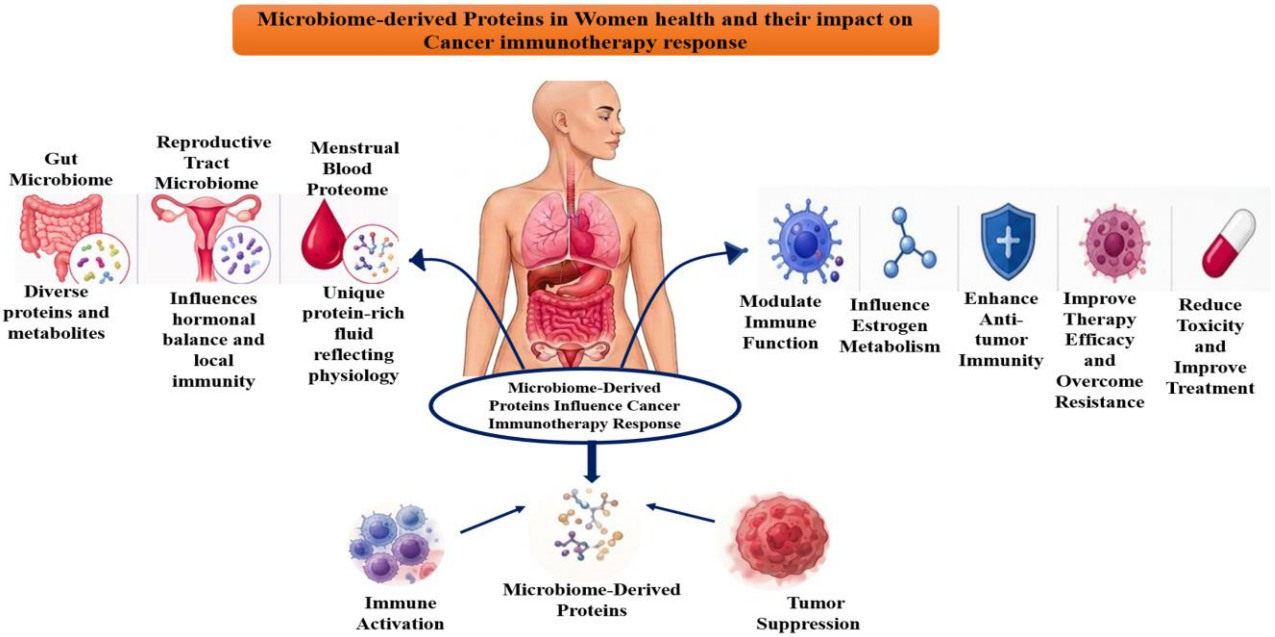
ABSTRACT

Background: Cancer progression and therapeutic response are influenced by tumor biology, host immunity, genetics, and the gut microbiome. Increasing evidence indicates that microbial composition and metabolites can modify inflammation, immune signaling, drug metabolism, and responses to cancer immunotherapy.
Objective: This review examines the role of the microbiome in cancer biology and immunotherapy and evaluates emerging engineering and computational technologies for investigating microbiome–immune–tumor interactions and supporting personalized therapeutic strategies.
Methods: Relevant evidence was synthesized across studies addressing microbiome–cancer interactions, microbiome–drug metabolism, stem cell-derived extracellular vesicles, organ-on-a-chip systems, tumor-on-a-chip platforms, microfluidic technologies, and in silico approaches. Particular emphasis was placed on physiologically relevant models capable of integrating microbial, immune, tumor, and therapeutic components.
Results: Gut microorganisms and their metabolites may influence tumor-associated inflammation, immune activation, epithelial integrity, drug metabolism, and immunotherapy response. Gut-on-a-chip and tumor-on-a-chip platforms can reproduce selected physiological and pathological features, including fluid flow, oxygen gradients, tissue interfaces, immune-cell interactions, and microbial signaling. Microfluidic systems further enable controlled co-culture, real-time monitoring, high-throughput screening, and assessment of therapeutic responses. Computational approaches, including molecular docking, molecular dynamics, protein-structure prediction, protein–protein interaction analysis, and machine learning, provide complementary tools for identifying therapeutic targets and predicting treatment responses.
Conclusion: Integrated microbiome engineering, microfluidics, organ-on-a-chip technologies, and computational approaches provide promising platforms for mechanistic cancer research, drug screening, and precision immunotherapy. However, standardization, scalability, regulatory requirements, reproducibility, and multicenter clinical validation remain important barriers to translation. Future integration with artificial intelligence, microbiome engineering, and patient-specific models may further advance individualized cancer treatment.

Keywords: Microfluidic chip, Gut microbiome, Cancer immunotherapy, organ-on-a-chip, precision oncology



INTRODUCTION

Cancer is a major global health burden, with substantial mortality and morbidity worldwide. The tumor microenvironment, host genetics, immune responses, and the microbiome all contribute to cancer development and progression.[1–3]

The gut microbiome has increasingly been recognized as an important factor in cancer biology, influencing treatment response, inflammation, metabolism, and immune regulation.[4–7] The interaction between the microbiome and cancer is particularly relevant in the context of emerging therapeutic strategies involving the modulation of microbial communities.[8–10]

Recent studies have also highlighted the potential role of stem-cell-derived extracellular vesicles in cancer research and therapeutic applications.[11–13] Mesenchymal stem/stromal cells and their extracellular vesicles may provide important biological cargo, including proteins, lipids, and nucleic acids, which can influence tumor-associated pathways.[14–16]

Organ-on-a-chip and microfluidic technologies provide additional platforms for investigating cancer biology under physiologically relevant conditions.[17–19] These systems can reproduce aspects of the tumor microenvironment and facilitate the study of cellular interactions, drug responses, and host–microbe relationships.[20–22]

Microbiome and Cancer

The gut microbiome is increasingly being investigated as a determinant of cancer development and therapeutic response.[23–25] Specific bacterial species and microbial metabolites may influence inflammation, immune signaling, epithelial integrity, and drug metabolism.[26–28]

Recent investigations have explored microbiome-based biomarkers and therapeutic approaches in oncology, including the potential use of microbial signatures for disease prediction and treatment stratification.[29–31]

Microbiome-Drug Interactions

Microbial metabolism can modify the activity, toxicity, and availability of anticancer drugs.[32] The intestinal microbiota may metabolize therapeutic compounds directly or indirectly influence drug efficacy through modulation of host metabolic and immune pathways.[33–34]

These interactions highlight the importance of considering the microbiome when evaluating pharmacological responses in cancer patients.[35]

Stem Cell-Derived Extracellular Vesicles and Cancer

Extracellular vesicles derived from mesenchymal stem/stromal cells have attracted considerable interest because of their ability to transport biologically active molecules between cells.[15,36] Their cargo may include proteins, lipids, messenger RNAs, microRNAs, and other regulatory molecules that can modify cellular behavior.[20,37]

Menstrual-blood-derived mesenchymal stromal cells and their extracellular vesicles have also been investigated as potential sources of therapeutic cargo.[20,38] These vesicles may provide opportunities for developing cell-free therapeutic strategies and investigating mechanisms of intercellular communication.[39,40].

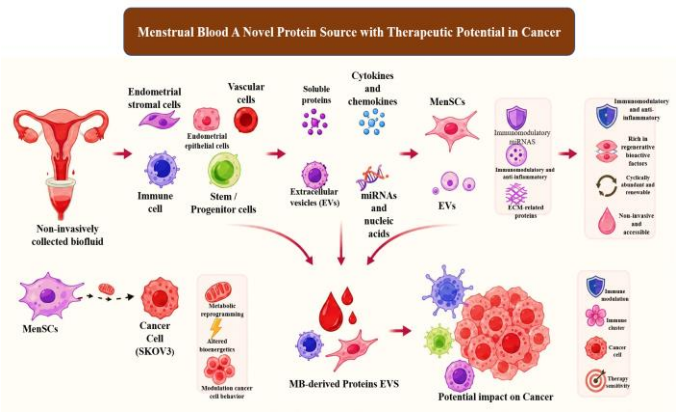


Figure.2 Different therapeutic potentials of Menstrual blood novel proteins

Gut-on-a-Chip Systems

The potential of engineering-based microbiome research has been further enhanced by the development of organ-on-a-chip technology. Organ-on-a-chip systems are micro-engineered devices that mimic the mechanical, structural and functional properties of human organs. These platforms arose as a response to the constraints of conventional cell culture models and animal studies, offering more physiologically appropriate alternatives for investigating human diseases.[42] Organ-on-a-chip technologies replicate tissue-specific design, molecular signaling and mechanical stresses necessary for normal organ function by incorporating living cells into microfluidic settings.[43] One of the most effective applications of this technology is the gut-on-a-chip which has developed into a useful model for examining microbiome-host interactions. The capacity of gut-on-a-chip devices to replicate important mechanical and physical characteristics of the intestinal environment is one of its distinguishing characteristics. Luminal contents and mechanical forces from peristaltic contractions constantly create fluid flow in the gastrointestinal system. These mechanical stimuli alter epithelial differentiation, mucus production, microbial colonization and immunological responses.[44] In order to replicate these physiological circumstances contemporary gut-on-a-chip technologies use cyclic mechanical deformation and regulated fluid flow producing more realistic experimental models than static cultures.[45] Furthermore, the creation of oxygen gradients makes it possible to cultivate anaerobic gut microbes and oxygen-dependent epithelial cells at the same time solving a significant problem in microbiome research.[46] The integration of anaerobic compartments inside gut-on-a-chip systems has been particularly important for investigating the human gut microbiota because many beneficial bacterial species cannot live under atmospheric oxygen levels. Advanced device designs maintain different oxygen conditions while preserving communication between microbial and host compartments. Additionally, these methods facilitate the development of mucosal interfaces that closely mimic those observed in vivo allowing for the study of barrier function, mucus interactions and microbial adherence. Through these advances gut-on-a-chip technology provides a comprehensive platform for exploring host–microbe interactions and microbial modulation of immune responses.[47,48] The utilization of gut-on-a-chip systems in cancer immunotherapy research is fast developing. These platforms make it possible to evaluate host immune cells, microbial communities and compounds produced from microbiomes in integrated experimental systems. Researchers can assess how responses to immune checkpoint inhibitors, cytokine treatments and novel immunotherapeutic approaches are affected by changes in microbiome makeup.[49] Additionally, the usage of gut-on-a-chip devices for drug screening and patient-specific therapeutic response prediction is growing. These technologies provide chances for customized microbiome diagnostics and treatment optimization by integrating patient-derived microbiota and immune cells.[50]

Tumor-on-a-Chip Technologies

The development of tumor-on-a-chip technology, which offers physiologically realistic platforms that faithfully replicate the intricacy of human tumors, has greatly revolutionized the study of cancer biology. Animal models might not accurately reflect human-specific responses and conventional two-dimensional cell cultures frequently fail to replicate the architectural, biochemical and mechanical features of tumor tissues.[41] By combining microfluidic engineering with living cancer cells, stromal elements, extracellular matrix components and immune cells within regulated microenvironments tumor-on-a-chip systems overcome these constraints. Key elements of the tumor microenvironment such as nutritional gradients, oxygen distribution, vascular networks and mechanical stressors that affect cancer growth and treatment responses can be replicated by researchers using these platforms.[51] The capacity of tumor-on-a-chip systems to create realistic tumor microenvironments is one of its main advantages. Highly diverse ecosystems with aberrant vasculature, hypoxia, acidic pH, immune infiltration and extracellular matrix remodeling are home to solid tumors. Together, these elements control treatment resistance, metastasis and tumor growth. Researchers can replicate physiological and pathological circumstances seen in vivo by precisely controlling these factors with microfluidic systems. For instance, it is possible to create oxygen and nutrient gradients inside microchannels to simulate hypoxic tumor areas and artificial extracellular matrices offer structural support that is similar to that of natural tissues. Compared to traditional culture methods these biomimetic circumstances enable more accurate investigation of cancer cell behavior and medication responses.[52,53] For the purpose of studying immune infiltration, microbiome-mediated signaling and treatment responses in cancer immunotherapy advanced tumor-on-a-chip technologies offer physiologically realistic platforms.

The use of tumor-on-a-chip systems for cancer immunotherapy research has been further enhanced by the integration of immune cells. Because the capacity of cytotoxic T lymphocytes, natural killer cells and antigen-presenting cells to enter tumor tissues directly affects anti-tumor activity, immune cell infiltration is a crucial factor in determining the efficacy of immunotherapy.[54] Under regulated conditions microfluidic technologies provide real-time monitoring of immune cell movement, activation and interactions with cancer cells. T-cell trafficking, immune checkpoint modulation and tumor immune evasion have all been studied using these models. Researchers can assess individualized immune responses and pinpoint elements that lead to immunotherapy resistance or sensitivity by combining patient-derived immune cells with tumor tissues.[55] The development of tumor-on-a-chip devices that can integrate microbial signals into cancer models has been spurred by the

increasing understanding of microbiome–tumor interactions. However, these intricate interactions are frequently not captured by conventional experimental setups. Researchers may now investigate how microbiome-derived variables impact cancer biology and treatment responses by integrating microbial metabolites, bacterial components and immune cells within tumor models thanks to sophisticated tumor-on-a-chip systems. For instance, short-chain fatty acids made by good gut bacteria can be added to microfluidic tumor systems to see how they affect tumor suppression and immune activation. The effect of pathogenic bacterial metabolites in responses may also be investigated.[56,57] Encouraging treatment resistance and immune evasion.[58] Drug resistance prediction is one of the most promising uses of tumor on-a-chip technology. In cancer, resistance to immune checkpoint inhibitors, targeted treatments and chemotherapy continues to be a significant problem. Due to the biochemical complexity of human malignancies conventional drug screening platforms often fail to predict clinical responses. By replicating patient-specific tumor features such as stromal connections, vascularization and immunological components tumor-on-a-chip systems get beyond this restriction. These platforms facilitate the identification of resistance mechanisms prior to clinical treatment and allow dynamic monitoring of cellular responses to therapeutic drugs. Integration of microbiome-derived metabolites into drug testing platforms may further increase predictive accuracy by accounting for the influence of gut bacteria on drug metabolism and immunity.

Microfluidics and Organ-on-a-Chip Technology

The development of tumor-on-a-chip technology which offers physiologically realistic platforms that faithfully replicate the intricacy of human tumors has greatly revolutionized the study of cancer biology. Animal models might not accurately reflect human-specific responses and conventional two-dimensional cell cultures frequently fail to replicate the architectural, biochemical and mechanical features of tumor tissues.[41] By combining microfluidic engineering with living cancer cells, stromal elements, extracellular matrix components and immune cells within regulated microenvironments, tumor-on-a-chip systems overcome these constraints. Key elements of the tumor microenvironment such as nutritional gradients, oxygen distribution, vascular networks and mechanical stressors that affect cancer growth and treatment responses can be replicated by researchers using these platforms.[51] The ability to create realistic tumor microenvironments is a key benefit of tumor-on-a-chip technologies. Highly diverse ecosystems with aberrant vasculature, hypoxia, acidic pH, immune infiltration and extracellular matrix remodeling are home to solid tumors. Together, these elements control treatment resistance, metastasis and tumor growth. Researchers can replicate physiological and pathological circumstances seen in vivo by precisely controlling these factors with microfluidic systems. For instance, it is possible to create oxygen and nutrient gradients inside microchannels to simulate hypoxic tumor areas and artificial extracellular matrices offer structural support that is similar to that of natural tissues. Compared to traditional culture methods, these biomimetic circumstances enable more accurate investigation of cancer cell behavior and medication responses.[52,53] According to Chen et al.[55] advanced tumor-on-a-chip systems offer physiologically relevant platforms for studying immune infiltration, derived immune cells with tumor tissues, personalized immune responses and factors that contribute to immunotherapy resistance or sensitivity Fig.2. The development of tumor-on-a-chip devices that can integrate microbial signals into cancer models has been spurred by the increasing understanding of microbiome tumor interactions. Through immunological modulation metabolite synthesis and inflammatory pathway regulation gut microbes have been shown in numerous studies to impact tumor growth.[59] However, these intricate interactions are frequently not captured by conventional experimental setups. Researchers may now investigate how microbiome-derived variables impact cancer biology and treatment responses by integrating microbial metabolites, bacterial components and immune cells within tumor models thanks to sophisticated tumor-on-a-chip systems. To assess their impact on immune activation, microbiome-mediated signaling and therapeutic responses in cancer immunotherapy. For instance, short-chain fatty acids generated by beneficial gut bacteria can be added to microfluidic tumor systems. The use of tumor-on-a-chip systems for cancer immunotherapy research has been further enhanced by the integration of immune cells. Because the capacity of cytotoxic T lymphocytes, natural killer cells and antigen-presenting cells to enter tumor tissues directly affects anti-tumor activity, immune cell infiltration is a crucial factor in determining the efficacy of immunotherapy.[54] Under regulated conditions microfluidic technologies provide real-time monitoring of immune cell movement, activation and interactions with cancer cells. T-cell trafficking, immune checkpoint modulation and tumor immune evasion have all been studied using these models. by incorporating tumor suppression for the patient. In a similar vein, it is possible to investigate how pathogenic bacterial metabolites contribute to immune evasion and treatment resistance.[58] Drug resistance prediction is one of the most promising uses of tumor on-a-chip technology. In cancer, resistance to immune checkpoint inhibitors, targeted treatments and chemotherapy continues to be a significant problem. Due to the biochemical complexity of human malignancies conventional drug screening platforms often fail to predict clinical responses. By replicating patient-specific tumor features, such as stromal connections, vascularization and immunological components tumor-on-a-chip systems get beyond this restriction. These platforms facilitate the identification of resistance mechanisms prior to clinical treatment and allow dynamic monitoring of cellular responses to therapeutic drugs. By taking into consideration the impact of gut microbes on medication metabolism and immunological responses, the incorporation of microbiome-derived metabolites into

drug testing systems may enhance predictive accuracy even more.[56,57]

Microfluidic devices manage fluid amounts in the nanolitre to microlitre range in channels that typically have a cross-section of 10–500 µm. In these geometries, flow is dominated by viscous forces (Re << 1), leading to stable, laminar, highly repeatable conditions that can be accurately predicted computationally.[60] After early microfluidic devices were composed of silicon or glass polydimethylsiloxane (PDMS) emerged as the material of choice for biological applications due to its optical transparency, gas permeability, biocompatibility and ease of soft-lithographic manufacture.[61] Organ-on-a-chip technologies go beyond simple microfluidics by merging living cells, controlled mechanical stimuli and multi-compartment designs to imitate tissue-level physiology.[22] Gut-on-a-chip devices mimic intestinal peristalsis and microbial co-culture.[62] Lung-on-a-chip devices capture the alveolar air-liquid interface and cyclic mechanical strain of breathing.[63] Tumor-on-a-chip systems mimic vascularized tumor microenvironments and drug penetration.[23] It is common practice to optimize channel geometry, predict wall shear stress and validate gradient generation prior to physical fabrication using computational fluid dynamics (CFD) simulation which uses Navier-Stokes solvers and species transport modules in COMSOL Multiphysics or ANSYS Fluent.[64]

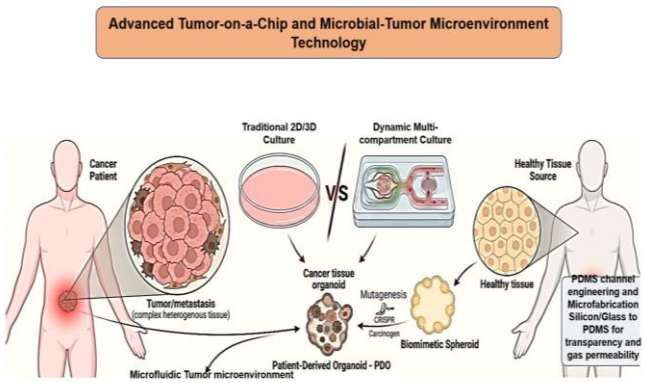


Fig.2 Tumor-on-a-chip systems offer physiologically relevant platforms for studying immune infiltration, derived immune cells with tumor tissues, personalized immune responses and factors that contribute to immunotherapy resistance or sensitivity

Microfluidic Technologies for Gut Microbiome Research

There is a pressing need for experimental platforms that can effectively replicate the intricate interactions between intestinal microbes, host tissues, immune cells and therapeutic drugs due to the growing acknowledgment of the gut microbiome as a critical predictor of cancer immunotherapy results. Although animal models and conventional in vitro culture systems have yielded important insights into microbiome biology, they frequently fall short of simulating the dynamic physiological conditions seen in the human gastrointestinal tract.[41] According to Kanniyappan et al.[42] microfluidic technologies have become potent engineering tools that allow for the precise manipulation of fluids, cells and microbes within microscale settings. Microfluidic platforms offer previously unheard-of capabilities to study microbiome-host interactions under extremely regulated and physiologically relevant circumstances by fusing biological and technical concepts.[43] The manipulation of minuscule fluid volumes via networked microchannels which are usually a few micrometers to several hundred micrometers in diameter, is known as microfluidics. Nutrient gradients, oxygen concentrations, pH, temperature and fluid shear stress are just a few of the environmental factors that can be precisely regulated thanks to this technology. These factors all have a significant impact on how microbes behave and how hosts react. Microfluidic devices in contrast to traditional static culture techniques, enable constant media perfusion and real-time biological process monitoring more closely simulating the dynamic environment of the human gut.[44] Additionally, high-throughput screening applications are made possible by the small amounts needed for experimentation which drastically cut reagent usage and operating costs. These benefits have established microfluidics as a revolutionary tool for researching intricate microbiome ecosystems and how they affect human health.[45] The capacity of microfluidic technology to accurately replicate gut ecology is one of its greatest contributions. The gastrointestinal tract is home to a variety of microbial communities that live in highly organized chemical and spatial gradients. It is difficult to replicate these conditions in conventional laboratory settings because fast growing species frequently take over microbial growth, reducing ecological complexity.[46] By facilitating the regulated compartmentalization and spatial organization of microbial populations, microfluidic technologies get beyond these restrictions. In order to facilitate the coexistence of aerobic, facultative anaerobic and obligatory anaerobic microbes in the same system researchers can create physiologically realistic oxygen gradients, nutrient distributions, and flow conditions.[47] The capacity of microfluidic systems to offer real-time monitoring of immunological and microbiological processes is another significant benefit. Microfluidic devices can be immediately combined with advanced imaging technologies, integrated biosensors and fluorescence-based detection techniques to provide continuous monitoring of molecular signaling events, cellular responses and microbiological development.[48] This ability is especially crucial for researching how the composition of the microbiota and immune activation alter over time during cancer treatment. Real-time analysis offers a more thorough understanding of microbiome-mediated treatment responses and allows researchers to record fleeting biological occurrences that would be overlooked in endpoint experiments.[49] Additionally, parallel research is made possible by microfluidic technologies which allow for the simultaneous testing of various microbial communities, medications or environmental conditions with the least amount of sample needed.[50] Additionally, microfluidic platforms are now essential instruments for studying host-microbe interactions. Researchers can directly study microbial colonization processes and their impact on host tissues by co-culturing intestinal epithelial cells with commensal or pathogenic microbes under physiologically relevant circumstances.[51] These investigations have provided important new understandings of mucosal immune responses, bacterial adhesion, epithelial barrier function and microbial metabolite synthesis. Our knowledge of how the gut microbiome affects immune regulation and the development of cancer has greatly increased thanks to the capacity to replicate the physical interfaces between microbes and host cells.[52] Another significant use of microfluidic technologies is the investigation of microbial colonization and biofilm formation. Microbial persistence, resistance to antimicrobial treatments, and chronic inflammation are all facilitated by biofilms which are highly ordered microbial populations embedded in extracellular polymeric matrices.

Biofilm production has been linked to colorectal cancer, inflammatory bowel illness and dysbiosis in the gastrointestinal system.[53] Controlled study of biofilm formation under dynamic flow conditions that closely mimic physiological settings is made possible by microfluidic devices. Researchers may assess how microbial communities interact with immune cells, create colonization niches, and react to environmental challenges. These investigations offer important insights into how biofilms affect treatment resistance and cancer immunotherapy results.[54] Microfluidics has emerged as a key platform for assessing medication reactions and therapeutic efficacy in addition to microbial ecology research. Pharmaceuticals, microbial metabolites and immunotherapeutic agents can be precisely delivered to cellular systems using this method, which also permits ongoing biological response monitoring. This ability is especially important in oncology where it is becoming more well acknowledged that the composition of the microbiome affects therapy outcomes. Researchers can examine how particular microbial species or metabolites affect reactions to immune checkpoint inhibitors, chemotherapy and combination therapies using microfluidic technologies. Developing microbiome-guided precision medicine methods to maximize treatment efficacy and minimize side effects requires this kind of knowledge.[55,56]

In Silico Computational Methods in Cancer Drug Discovery

In silico genomic analysis combined with molecular docking may identify bacterial secondary metabolites with anticancer potential as demonstrated by the screening of Bacillus sp., strain MHSD_37 metabolites against fibroblast growth factor.[57] AlphaFold2 predicts single-chain protein structures with almost experimental accuracy.[58] This ability is extended to protein ligand and protein–protein complexes by AlphaFold3 enabling more detailed structural modeling of biomolecular interactions.[59] AutoDock Vina provides rapid and confirmed molecular docking with binding affinity prediction in kcal/mol[60] whereas HADDOCK permits data-driven protein–protein docking by incorporating experimental biochemical limitations.[61] GROMACS molecular dynamics (MD) simulations are used to optimize docking poses, estimate binding free energies using the Molecular Mechanics Generalized Born Surface Area (MM-GBSA) approach, and describe conformational dynamics over timeframes of 50–200 ns.[62,63] Building and analyzing protein–protein interaction (PPI) networks with STRING and Cytoscape facilitates hub protein identification and pathway enrichment analysis.[64,65] Furthermore, machine learning classifiers trained on multi-omics microbiome data have demonstrated strong predictive performance with an area under the receiver operating characteristic curve (AUC) exceeding 0.80 for the prediction of immune checkpoint inhibitor (ICI) response.[66]

DISCUSSION

The extensive use of microfluidics, organ-on-a-chip technologies, biosensors and three-dimensional bioprinting in microbiome-guided cancer immunotherapy research and clinical practice is still hampered by a number of translational issues. The lack of uniformity among experimental platforms is one of the biggest drawbacks. To create broadly applicable experimental models and biomarkers different labs often use different device layouts, fabrication materials, cell sources and culture conditions. Another significant barrier to the widespread application of engineering-based biomedical systems is manufacturing difficulties. Numerous organ-on-a-chip and tumor-on-a-chip systems need highly controlled manufacturing settings, specific materials and advanced fabrication procedures. While remarkable proof-of-concept models have been created by university labs, scaling these technologies for analytical techniques has led to significant diversity in experimental results. These discrepancies make it more difficult to compare data and lower reproducibility, which is nonetheless a crucial prerequisite for both scientific validation and regulatory approval. Additionally, individual differences in microbiota composition add to the complexity, making commercial manufacturing both economically and technically challenging. Their practical application is further hampered by device-to-device variability, low durability and challenges in sustaining long-term microbial cultures. Similar issues with bioink optimization, printing resolution, structural stability and cell viability preservation frequently arise in three-dimensional bioprinting methods all of which have an impact on model dependability and translational potential. Another significant obstacle is regulatory hurdles. Current regulatory frameworks are ill-suited to assess intricate bioengineered systems that incorporate living cells, microbes and artificial intelligence-based analytical techniques because they were mostly created for traditional pharmaceuticals and medical devices. The absence of established validation criteria increases uncertainties regarding safety evaluation, quality control and clinical application. Additionally, the utilization of patient-derived tissues and microbiota presents ethical and regulatory considerations pertaining to informed permission, data privacy and biological sample storage. Clinical translation and commercialization of these new technologies will be made easier with the establishment of clear regulatory criteria. One of the most crucial but still undeveloped facets of microbiome-engineering research is clinical validation. Relatively few technologies have undergone thorough clinical testing, despite the fact that many research have shown encouraging outcomes in laboratory conditions. To verify the clinical value, predictive accuracy and dependability of microbiome-based engineering platforms, extensive, multicenter validation studies are needed. Furthermore, therapeutic responses might be greatly impacted by patient heterogeneity, variations in microbiome composition, lifestyle factors, dietary habits and genetic backgrounds which calls for thorough validation across a range of populations. The move from experimental models to standard clinical applications will remain restricted in the absence of strong clinical proof. tumor microenvironments and microbial communities in a single dynamic apparatus. These cutting-edge platforms will offer previously unheard-of chances to study intricate host-microbe relationships and forecast patient-specific reactions to immunotherapeutic treatments. Through the creation of synthetic microbial consortia, engineered probiotics and microbiome-editing techniques meant to boost anti-tumor immunity, certain methods could be applied to human microbiome research. Future organ-on-a-chip systems that incorporate nanotechnology may make it possible to monitor microbial metabolites, immunological biomarkers and tumor-derived signals in real time with hitherto unheard-of sensitivity. These nano-enabled systems could help identify resistance mechanisms, optimize therapeutic treatments and predict treatment response early. Furthermore, the rational design of synthetic microbiomes suited for therapeutic purposes may be made easier by growing knowledge of microbial interactions and community dynamics. In the end, it is anticipated that the combination of modern engineering technologies, artificial intelligence and microbiome research will change cancer immunotherapy from a population-based strategy to a genuinely customized treatment paradigm. It will take interdisciplinary cooperation amongst microbiologists, oncologists, engineers, computer scientists and nanotechnologists to create clinically proven platforms that can enhance patient outcomes and treatment efficacy in order to realize this ambition. So, it

concluded that through controlling immune activation, microbial metabolite production and microenvironment dynamics the gut microbiome significantly influences the results of cancer immunotherapy. Beneficial microbial taxa and their metabolites might improve therapeutic efficacy while dysbiosis may lead to treatment resistance, as this tumor review emphasizes. Advanced engineering technologies, including microfluidics, gut-on-a-chip, tumor-on-a chip have considerably increased our ability to predict and study microbiome–immune–tumor interactions under physiologically realistic conditions. These platforms offer important chances for response prediction, drug screening, mechanistic research, microbiome discoveries into individualized cancer treatment and bettering patient outcomes.

Future Perspectives

Microbiology, biomedical engineering, nanotechnology, artificial intelligence and precision medicine will probably come together to form the future of microbiome-guided cancer immunotherapy. By combining host tissues, immune cells, microbial communities, and tumor microenvironments into a single dynamic device emerging microbiome-on-a-chip platforms are anticipated to represent the next generation of experimental systems. These cutting-edge platforms will offer previously unheard-of chances to study intricate host-microbe interactions and forecast patient-specific reactions to immunotherapeutic treatments. Through the creation of synthetic microbial consortia, engineered probiotics and microbiome-editing techniques targeted at boosting anti-tumor immunity certain methods could be applied to human microbiome research. Future oncology integration with organ-on-a-chip systems may allow for hitherto unheard-of sensitivity in real-time monitoring of immunological biomarkers, microbial metabolites and tumor-derived signals. These mechanically designed platforms may make it easier to identify resistance mechanisms, predict therapy response early and optimize therapeutic approaches. Ultimately, it is expected that the integration of microbiome research and state-of-the-art engineering technologies would transform cancer immunotherapy from a population-based approach to a truly tailored treatment paradigm. To achieve this goal, microbiologists, oncologists, engineers and computer scientists must collaborate across disciplines to create clinically validated platforms that can improve patient outcomes and treatment efficacy.

CONCLUSION

Through controlling immune activation, microbial metabolite synthesis and tumor microenvironment dynamics, the gut microbiome significantly influences the results of cancer immunotherapy. This study emphasizes that while dysbiosis may lead to treatment resistance, beneficial microbial taxa and their metabolites might improve therapeutic efficiency. Microfluidics, gut-on-a-chip and tumor-on-a-chip are examples of advanced engineering technologies that have greatly enhanced our capacity to simulate and examine microbiota–immune–tumor interactions under physiologically realistic settings. These platforms offer important chances for drug screening, response prediction, mechanistic research and the creation of tailored treatments. Despite encouraging developments, before widespread clinical usage, issues with standardization, scalability, regulatory approval and clinical validation must be resolved. The advancement of precision immunotherapy is anticipated to be accelerated by the future combination of microbiome-on-a-chip devices, artificial intelligence and microbiome engineering techniques. The combination of mechanical engineering and microbiology provides a revolutionary foundation for converting microbiome findings into individualized cancer treatment and enhancing patient outcomes.

Ethical Approval

Ethical approval was not required for this narrative review because it involved the synthesis and analysis of previously published literature and did not involve human participants, animals, or the collection of primary data.

Data Availability

No new datasets were generated or analyzed during this narrative review. The review was based on previously published literature and publicly available information.

Author Contributions

Conceptualization: Muqadas Munir, Hasnain Jadoon
Literature Review and Analysis: Muqadas Munir, Hasnain Jadoon, Tanveer Hussain, Harmain Munir
Writing – Original Draft: Muqadas Munir, Hasnain Jadoon
Writing – Review & Editing: Muqadas Munir, Hasnain Jadoon, Tanveer Hussain, Harmain Munir
Final Approval: All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Informed Consent

Informed consent was not applicable because this study did not involve human participants or the collection of personal data.

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Conflict of Interest

The authors declare that they have no competing interests.

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Declaration of AI-Assisted Language Editing

ChatGPT was used for grammar and language correction then verified by the authors.

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