Journal of Advanced Research in Dental & Oral Health
Volume 10, Issue 1&2 - 2025, Pg. No. 1-7
Peer Reviewed & Open Access Journal

Review Article

Therapeutic Targets in Biofilm-Mediated Oral Cancer: Innovations and Challenges

Dhanvin Hetarth Patel[1], Kunal Vora[2], Shreosee Ghosh[3]

[1]GEMS Modern Academy, Nad Al Sheba, Dubai, United Arab Emirates
[2,3]SHRM Biotechnologies Pvt. Ltd., Madhyamgram, Kolkata, West Bengal
DOI: https://doi.org/10.24321/2456141X.202501

I N F O

Corresponding Author:
Shreosee Ghosh, SHRM Biotechnologies Pvt. Ltd., Madhyamgram, Kolkata, West Bengal
E-mail Id:
Shreoseeghosh@gmail.com
Orcid Id:
https://orcid.org/0009-0001-4518-9869
How to cite this article:
Patel D H, Vora K, Ghosh S. Therapeutic Targets in Biofilm-Mediated Oral Cancer: Innovations and Challenges. J Adv Res Dent Oral Health. 2025; 10(1&2): 1-7.

Date of Submission: 2025-01-07
Date of Acceptance: 2025-02-12

A B S T R A C T

Oral cancer remains a major global health challenge, with increasing evidence linking microbial biofilms to tumour initiation, progression, and therapy resistance. Biofilms contribute to a pro-inflammatory and immunosuppressive microenvironment, fostering cancer stem cell survival and tumour aggressiveness. This review explores biofilm dynamics in oral cancer, highlighting key molecular targets (MAPK, NF-κB) and innovative therapies such as quorum-sensing inhibitors, nanotechnology-based drug delivery, and immunotherapy. Challenges include treatment resistance, biofilm heterogeneity, and translational barriers. Future research must focus on multi-targeted therapies, personalised medicine, and AI-driven drug discovery to revolutionise biofilm-mediated oral cancer treatment.

Keywords: Oral Cancer, Biofilms, Biofilm-Mediated Tumorigenesis, Quorum Sensing, Chronic Inflammation

Introduction

Oral cancer is one of the most common cancers globally, ranking among the top ten malignancies, with its highest prevalence in South Asia, parts of Europe, and Latin America. According to recent data, oral squamous cell carcinoma (OSCC) constitutes over 90% of all oral cancer cases, with an alarming annual incidence of approximately 377,000 new cases and 177,000 deaths worldwide. The disease's multifaceted aetiology involves a combination of genetic, environmental, and lifestyle factors, such as tobacco use, alcohol consumption, and areca nut chewing. Furthermore, emerging evidence has highlighted the role of microbial biofilms in exacerbating the initiation and progression of oral cancer, underscoring a need for novel therapeutic approaches.[1,2]

Biofilms are highly organised microbial consortia that adhere to biotic or abiotic surfaces, encased in a self-produced extracellular polymeric substance (EPS). This EPS matrix confers remarkable structural and functional advantages to biofilms, including resistance to antimicrobial agents and host immune responses. Biofilms are dynamic ecosystems, exhibiting cellular heterogeneity, metabolic specialisation, and intercellular communication via quorum-sensing (QS) mechanisms. These sophisticated systems enhance the survival, virulence, and adaptability of microbial communities under hostile conditions.[3]

In the context of oral cancer, biofilms play a pivotal role in creating a tumour-promoting microenvironment. Persistent colonisation of oral surfaces by microbial biofilms leads to chronic inflammation, dysregulated immune responses, and the release of carcinogenic metabolites. These processes facilitate cellular transformation, proliferation, and migration, which are hallmarks of oncogenesis. Furthermore, biofilm-associated microorganisms can modulate epithelial-mesenchymal transition (EMT), a critical step in metastasis, and support the survival of cancer stem cells (CSCs), which are closely associated with tumour recurrence and therapeutic resistance.[4]

Recent studies have elucidated key molecular pathways and targets involved in biofilm-mediated oral cancer, for instance, biofilm-related inflammation is driven by the activation of signalling pathways such as nuclear factor kappa B (NF-κB), mitogen-activated protein kinase (MAPK), and phosphatidylinositol 3-kinase (PI3K/AKT). These pathways orchestrate the production of pro-inflammatory cytokines, angiogenic factors, and matrix metalloproteinases, which collectively promote tumour growth and invasion[5]. Additionally, genetic alterations in biofilm-associated microbial communities, including horizontal gene transfer and the acquisition of antibiotic-resistance genes, further complicate the clinical management of biofilm-mediated oral cancer.[6]

Despite advancements in understanding biofilm biology, targeting biofilm-mediated mechanisms in oral cancer remains a significant challenge. Conventional therapies such as surgery, radiation, and chemotherapy show limited efficacy against biofilm-associated tumours due to the protective nature of the EPS matrix and the inherent heterogeneity of biofilms. Innovative approaches, including quorum-sensing inhibitors, antimicrobial peptides, and nanoparticle-based drug delivery systems, have demonstrated potential in preclinical studies but face translational barriers in clinical settings.[7]

This review aims to provide a comprehensive analysis of biofilm-mediated oral cancer, focusing on the mechanisms by which biofilms influence tumour progression, immune modulation, and therapeutic resistance. It highlights recent advancements in identifying molecular and cellular targets and evaluates emerging therapeutic strategies. By integrating insights from microbiology, oncology, and bioinformatics, this paper seeks to foster a deeper understanding of biofilm-mediated oncogenesis and explore innovative approaches to mitigate its impact, thereby addressing an urgent unmet need in cancer therapy.

Biofilm Dynamics in Oral Cancer

Biofilms are intricate microbial communities that form on biotic and abiotic surfaces, including those in the oral cavity. These structures are encased within a self-produced extracellular polymeric substance (EPS) matrix, which confers remarkable resilience against environmental stressors, antimicrobial agents, and host immune responses. In the oral cavity, biofilms play a dual role: while they contribute to maintaining oral homeostasis under healthy conditions, their dysregulation has been implicated in various pathological conditions, including oral cancer.

Mechanisms of Biofilm Formation in the Oral Cavity

Biofilm formation is a multi-step process involving initial attachment, irreversible adhesion, maturation, and dispersal. In the oral cavity, initial attachment begins with the reversible adhesion of planktonic microbial cells to salivary pellicle-coated surfaces, such as teeth, tongue, and mucosal epithelium. This phase is mediated by weak interactions, including van der Waals forces and hydrophobic interactions, and is influenced by environmental factors such as pH, temperature, and nutrient availability.[3]

Once attached, microbial cells transition to irreversible adhesion through the production of appendages like fimbriae and pili, which anchor them to the substrate. This stage is marked by the secretion of the EPS matrix, composed of polysaccharides, proteins, and extracellular DNA (eDNA). The maturation phase is characterised by the development of complex three-dimensional architectures with spatial heterogeneity in nutrient distribution and metabolic activity. Finally, dispersal involves the detachment of microbial cells, facilitating biofilm propagation to new sites.[8]

Interactions between Oral Biofilms and Epithelial Tissues

Oral biofilms establish dynamic and often antagonistic interactions with epithelial tissues. Healthy oral biofilms maintain a balanced microbial ecosystem, contributing to the integrity of epithelial barriers and local immune homeostasis. However, pathogenic biofilms, dominated by virulent microorganisms, disrupt this balance, leading to chronic inflammation and tissue damage.

Pathogenic biofilms secrete enzymes like proteases and lipases that degrade epithelial barriers, increasing permeability and facilitating microbial invasion. Furthermore, biofilms release pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α), which activate immune cells and perpetuate inflammation. This chronic inflammatory state creates a pro-tumorigenic microenvironment conducive to genetic instability, cellular transformation, and angiogenesis.[5]

Contribution of Biofilms to Tumorigenesis and Cancer Progression

Biofilms contribute to tumorigenesis through multiple mechanisms, including chronic inflammation, immune modulation, and metabolic dysregulation. Persistent biofilm presence in the oral cavity induces the release of reactive oxygen species (ROS) and nitrogen species (RNS), which damage DNA and promote mutagenesis. Additionally, the biofilm-associated microenvironment supports epithelial-mesenchymal transition (EMT), a critical process in cancer metastasis.[9,10]

Quorum sensing, a key communication mechanism in biofilms, regulates the expression of virulence factors and biofilm maturation. QS molecules, such as autoinducer-2, have been shown to influence host cellular pathways, including those governing cell proliferation and apoptosis.

ISSN: 2456-141X
DOI: https://doi.org/10.24321/2456141X.202501

Biofilms also protect cancer stem cells (CSCs), which are central to tumour recurrence and therapy resistance, by providing a hypoxic and nutrient-rich microenvironment that enhances CSC survival and plasticity.[2,11]

Emerging evidence suggests that biofilm-associated microorganisms produce carcinogenic metabolites, such as acetaldehyde and nitrosamines, which further contribute to oral carcinogenesis. Moreover, horizontal gene transfer within biofilm communities facilitates the dissemination of oncogenic and antibiotic-resistance genes, compounding the complexity of treating biofilm-mediated oral cancers.[6]

In summary, oral biofilms play a multifaceted role in cancer initiation and progression by modulating the local microenvironment, interacting with epithelial tissues, and influencing key oncogenic pathways. Understanding these dynamics is crucial for developing targeted interventions aimed at mitigating the oncogenic potential of biofilms in oral cancer.

Molecular and Cellular Targets in Biofilm-Mediated Oral Cancer

The intricate interplay between biofilms and oral cancer progression is orchestrated through various molecular and cellular mechanisms. Understanding these targets is essential for designing effective therapeutic interventions.

Key Molecular Targets

Signalling Pathways Involved

- **MAPK Pathway:** The mitogen-activated protein kinase (MAPK) pathway is activated in response to inflammatory mediators and microbial signals from biofilms. It regulates the expression of pro-inflammatory cytokines, such as interleukin-6 (IL-6), and drives cell proliferation and survival, contributing to tumour growth.[5]
- **NF-κB Pathway:** Chronic biofilm-mediated inflammation activates nuclear factor kappa B (NF-κB), a pivotal regulator of immune responses, apoptosis, and cell cycle progression. Persistent activation of NF-κB promotes angiogenesis and metastasis, thereby facilitating cancer progression.[10]
- **PI3K/AKT Pathway:** The phosphatidylinositol 3-kinase (PI3K)/AKT pathway is implicated in cell survival, metabolism, and invasion. Biofilm-associated signalling molecules induce the PI3K/AKT pathway, enhancing resistance to apoptosis and promoting epithelial-mesenchymal transition (EMT).[4]

Key Biomarkers

- **Interleukin-6 (IL-6):** Elevated levels of IL-6 are associated with biofilm-induced inflammation, creating a pro-tumorigenic microenvironment. IL-6 activates downstream signalling, including the STAT3 pathway, which enhances cancer cell proliferation and immune evasion.[9]
- **Vascular Endothelial Growth Factor (VEGF):** VEGF is upregulated in biofilm-mediated oral cancer, promoting angiogenesis and facilitating tumour growth and metastasis.[6]
- **Matrix Metalloproteinases (MMPs):** Biofilms stimulate the secretion of MMPs, particularly MMP-2 and MMP-9, which degrade the extracellular matrix and enhance tumour invasion and metastasis.[7]
- **Reactive Oxygen Species (ROS):** Chronic biofilm-induced oxidative stress leads to the accumulation of ROS, resulting in DNA damage and mutagenesis. ROS also modulate signalling pathways that promote tumour survival and growth.[5]

Cellular Mechanisms

Immune Evasion by Biofilms

Biofilms create a robust EPS matrix that shields microbial communities from host immune defences. This matrix limits the penetration of immune cells, such as neutrophils and macrophages, reducing their efficacy. Biofilms also secrete immunosuppressive molecules, including prostaglandins and anti-inflammatory cytokines, which dampen immune responses. Additionally, biofilm-mediated chronic inflammation leads to immune exhaustion, characterised by the impaired function of T cells and natural killer (NK) cells, further enabling tumour progression.[10]

Cancer Stem Cells (CSCs) Within Biofilm-Associated Niches

Cancer stem cells (CSCs) are a subpopulation of tumour cells with self-renewal and differentiation capabilities, critical for tumour initiation, progression, and recurrence. Biofilm-associated niches provide an ideal microenvironment for CSC survival and proliferation. Hypoxia within biofilm microenvironments enhances the expression of stemness markers, such as CD44 and ALDH1, and activates signalling pathways like Hedgehog and Wnt/ β-catenin, which are pivotal for maintaining CSC phenotypes. Furthermore, biofilm-mediated immune suppression protects CSCs from immune surveillance, contributing to therapeutic resistance[6,11]

Therapeutic Implications

Targeting these molecular and cellular mechanisms offers a promising avenue for mitigating biofilm-mediated oral cancer. Strategies include inhibitors of MAPK, NF-κB, and PI3K/AKT pathways, as well as agents targeting VEGF and MMPs to disrupt angiogenesis and invasion. Additionally, therapies aimed at reactivating immune responses and disrupting CSC niches hold the potential for improving treatment outcomes.

ISSN: 2456-141X
DOI: https://doi.org/10.24321/2456141X.202501

Current Therapeutic Approaches

The management of biofilm-associated oral cancers poses significant challenges due to the protective nature of biofilms and their contribution to therapeutic resistance. While conventional therapies remain the cornerstone of oral cancer treatment, emerging therapeutic approaches targeting biofilm-mediated mechanisms offer promising alternatives.

Conventional Therapies and Their Limitations

The primary modalities for treating oral cancer include surgical resection, radiation therapy, and chemotherapy. Surgical resection aims to remove localised tumours, while radiation and chemotherapy target residual cancer cells and metastatic lesions. However, these conventional therapies exhibit limited efficacy in biofilm-associated oral cancers for several reasons.

Biofilm-associated tumours benefit from the protective extracellular polymeric substance (EPS) matrix, which acts as a barrier to therapeutic agents. Additionally, the heterogeneous metabolic states and genetic adaptability of biofilm-resident cells enhance their resistance to cytotoxic drugs and radiation. Cancer stem cells (CSCs), which thrive in the hypoxic and nutrient-rich microenvironment of biofilms, further contribute to tumour recurrence and treatment failure.[6,13]

Emerging Therapies Targeting Biofilm-Mediated Mechanisms

Antimicrobial Peptides and Quorum-Sensing Inhibitors

Antimicrobial peptides (AMPs) represent a promising strategy for targeting biofilms in oral cancer. These small, naturally occurring molecules exhibit potent activity against microbial communities by disrupting membrane integrity and interfering with biofilm formation. Additionally, synthetic AMPs can be engineered to enhance specificity and reduce toxicity.

Quorum-sensing inhibitors (QSIs) disrupt microbial communication within biofilms, impairing their ability to coordinate virulence and resistance mechanisms. Compounds like furanones and synthetic analogues have demonstrated efficacy in preclinical studies by inhibiting quorum-sensing pathways and reducing biofilm biomass. QSIs also sensitise biofilms to conventional antimicrobials, offering a synergistic therapeutic approach.[8]

Nanoparticle-Based Drug Delivery Systems

Nanoparticle-based drug delivery systems have emerged as a cutting-edge approach to overcome the limitations of conventional therapies. These systems leverage nanoscale carriers to deliver therapeutic agents directly to biofilms, enhancing drug penetration and efficacy.

Nanoparticles can be functionalised with biofilm-targeting ligands, such as peptides or antibodies, to improve specificity. Additionally, they can encapsulate chemotherapeutic drugs, AMPs, or QSIs, providing sustained release and reducing systemic toxicity. For example, silver and gold nanoparticles have shown significant anti-biofilm and anti-cancer activity in experimental models.[7]

Immunotherapy and Integration with Anti-Biofilm Strategies

Immunotherapy, which harnesses the immune system to combat cancer, has revolutionised oncology. However, its application in biofilm-associated oral cancers is hindered by the immunosuppressive microenvironment created by biofilms.

Recent advances have explored the integration of anti-biofilm strategies with immunotherapy. For instance, disrupting the biofilm matrix with enzymes or AMPs can expose microbial and tumour antigens, enhancing immune recognition. Immune checkpoint inhibitors, such as anti-PD-1/ PD-L1 antibodies, combined with biofilm-targeting agents, have shown potential in preclinical models by reactivating immune responses and reducing tumour burden.[2]

The convergence of biofilm-targeting strategies with advanced therapeutic modalities, such as CRISPR-Cas9 and RNA-based therapeutics, holds immense potential for overcoming the challenges posed by biofilm-associated cancers. A multidisciplinary approach integrating molecular biology, nanotechnology, and immunology is essential for translating these innovations into clinical practice.

Challenges in Targeting Biofilm-Mediated Oral Cancer

Targeting biofilm-mediated oral cancer presents significant challenges that stem from the inherent complexity of biofilms, their interactions with host tissues, and limitations in current therapeutic approaches. Despite advancements in understanding the molecular mechanisms underlying biofilm-associated malignancies, several obstacles hinder the development of effective treatments.

Resistance to Conventional Therapies

Biofilm-mediated oral cancer is notoriously resistant to conventional therapies such as surgery, chemotherapy, and radiotherapy. The extracellular polymeric substance (EPS) matrix of biofilms acts as a physical and biochemical barrier, limiting the penetration of therapeutic agents. Additionally, biofilm-associated cells exhibit altered metabolic states, reduced growth rates, and enhanced expression of efflux pumps, further diminishing the efficacy of chemotherapeutic drugs [3]. This resistance often necessitates higher doses of treatment, leading to increased toxicity and adverse effects in patients.[7]

ISSN: 2456-141X
DOI: https://doi.org/10.24321/2456141X.202501

Heterogeneity of Biofilm Communities

The structural and functional heterogeneity within biofilm communities poses a critical challenge in designing effective treatments. Biofilms in oral cancer are composed of diverse microbial species, each contributing uniquely to the tumour microenvironment. This microbial diversity fosters the emergence of metabolically distinct subpopulations with varying susceptibilities to therapeutic agents [2]. Furthermore, the spatial organisation of biofilms, with gradients of nutrients and oxygen, creates microenvironments that support cellular adaptation and survival under stress. This heterogeneity complicates the development of targeted therapies and often results in incomplete eradication of biofilms, contributing to tumour recurrence.

Toxicity and Side Effects of Emerging Therapeutics

Although innovative approaches such as quorum-sensing inhibitors, antimicrobial peptides, and nanoparticle-based drug delivery systems have shown promise in preclinical studies, their clinical application is often limited by toxicity and side effects. Many of these emerging therapies lack specificity, potentially affecting non-target cells and tissues, for instance, certain antimicrobial peptides can disrupt host cell membranes, leading to cytotoxic effects [5]. Similarly, the use of nanoparticles raises concerns about long-term biocompatibility and potential systemic toxicity, which need to be carefully evaluated before clinical implementation.[6]

Challenges in Translating Preclinical Findings to Clinical Applications

Bridging the gap between preclinical research and clinical application remains a formidable challenge in biofilm-mediated oral cancer therapy. Many preclinical studies rely on in vitro or animal models that fail to fully replicate the complexity of human biofilms and their interactions with host tissues. Additionally, the lack of standardised protocols for biofilm disruption and therapeutic evaluation hinders the reproducibility of findings across studies.[8] Clinical trials often face logistical challenges, including patient recruitment, ethical considerations, and the high cost of evaluating novel therapies. These barriers significantly delay the translation of promising research into effective clinical treatments.

Addressing these challenges requires a multidisciplinary approach that integrates advances in molecular biology, nanotechnology, and clinical oncology. Efforts should focus on improving the specificity and efficacy of emerging therapeutics, developing robust models for preclinical studies, and fostering collaboration between researchers and clinicians to accelerate translational research. By overcoming these obstacles, the field can advance toward more effective strategies for managing biofilm-mediated oral cancer.[12]

Future Perspectives

The management of biofilm-mediated oral cancer requires innovative strategies to overcome the inherent complexities of biofilm-associated resistance, heterogeneity, and tumour-promoting capabilities. Future directions in this field emphasise multi-targeted therapeutic approaches, the integration of artificial intelligence (AI) and machine learning (ML) for therapeutic optimisation, personalised medicine, and the development of combinatorial therapies.

Advancing Multi-Targeted Therapeutic Strategies

Targeting biofilm-mediated oral cancer necessitates addressing multiple molecular pathways and cellular mechanisms simultaneously. Biofilms contribute to a tumorigenic microenvironment by activating inflammatory cascades, immune evasion mechanisms, and cancer stem cell (CSC) niches. Multi-targeted therapeutic strategies aim to disrupt these interconnected processes. For example, the combined inhibition of NF-κB and PI3K/AKT signalling pathways has shown promise in preclinical models by attenuating biofilm-induced inflammation and tumour proliferation [5]. The development of therapies that simultaneously target biofilm structural integrity, quorum sensing, and microbial virulence factors could provide comprehensive solutions to overcome the limitations of monotherapies.

Role of Artificial Intelligence and Machine Learning in Therapeutic Optimisation

The application of AI and ML offers transformative potential in the optimisation of therapeutic strategies against biofilm-mediated oral cancer. AI-driven drug discovery platforms have identified novel quorum-sensing inhibitors with enhanced specificity. Additionally, machine learning models are being used to predict patient responses to biofilm-targeting therapies, enabling personalised treatment plans. Future developments may include AI-assisted imaging for real-time monitoring of biofilm formation in cancerous tissues, aiding in early diagnosis and treatment efficacy assessment.

Importance of Personalised Medicine

Personalised medicine offers a paradigm shift in treating biofilm-mediated oral cancer by tailoring interventions to the unique genetic, molecular, and microbial profiles of individual patients. Advances in next-generation sequencing and multi-omics technologies have enabled the identification of patient-specific biofilm compositions and their functional impact on the tumour microenvironment [6]. Such insights can inform the design of precision therapeutics targeting the specific microbial communities and signalling pathways relevant to each case.[13] Personalised approaches may also include the use of patient-derived organoids and

ISSN: 2456-141X
DOI: https://doi.org/10.24321/2456141X.202501

biofilm-on-chip models to predict treatment responses in vitro, facilitating the selection of optimal therapeutic combinations.

Potential for Combinatorial Therapies

The inherent resilience of biofilm-mediated oral cancer underscores the need for combinatorial therapeutic strategies that leverage synergistic mechanisms. Combining biofilm disruptors, such as quorum-sensing inhibitors or enzymatic EPS degraders, with immune modulators could enhance the efficacy of immunotherapy by restoring immune surveillance in the tumour microenvironment [7]. Additionally, nanotechnology-based drug delivery systems offer a platform for co-delivering multiple therapeutic agents directly to biofilm-associated tumours, ensuring sustained release and targeted action. Combinatorial approaches have demonstrated significant potential in preclinical studies, particularly when integrating traditional chemotherapeutics with biofilm-targeted interventions.

The future of biofilm-mediated oral cancer treatment lies in the convergence of multi-targeted strategies, technological innovations, and personalised medicine. By integrating advancements in AI, molecular biology, and drug delivery systems, researchers can develop more effective therapies that address the unique challenges posed by biofilms. Collaborative, interdisciplinary efforts will be critical in translating these innovations into clinical practice, ultimately improving outcomes for patients affected by this complex and challenging disease.

Conclusion

This review highlights the intricate interplay between biofilms and oral cancer, emphasising their role in promoting tumorigenesis, therapeutic resistance, and immune evasion. Biofilms, as complex microbial ecosystems, contribute significantly to the progression of oral cancer by fostering chronic inflammation, enhancing the survival of cancer stem cells, and modulating the tumour microenvironment. Key findings from recent studies underscore the multifaceted nature of biofilm-mediated mechanisms, including the activation of oncogenic signalling pathways such as NF-κB and PI3K/AKT, the acquisition of genetic adaptability, and the emergence of treatment-resistant microbial communities.

Addressing the challenges posed by biofilm-mediated oral cancer requires a shift toward multi-targeted therapeutic strategies that integrate biofilm disruptors, immune modulators, and advanced drug delivery systems. Moreover, the application of artificial intelligence and machine learning offers transformative potential for identifying novel therapeutic targets, optimising treatment regimens, and advancing personalised medicine. Combinatorial therapies, leveraging synergistic mechanisms, hold promise in overcoming the limitations of current monotherapies and improving patient outcomes.

Despite these advancements, significant gaps remain in understanding the complex dynamics of biofilms within the oral cancer microenvironment. The inherent heterogeneity of biofilms and their adaptive capabilities continue to pose challenges in developing universally effective therapeutic strategies. This underscores the need for interdisciplinary research that bridges molecular microbiology, oncology, bioinformatics, and translational medicine. Collaborative efforts among researchers, clinicians, and data scientists will be essential to unravel the complexities of biofilm-associated oncogenesis and translate emerging therapies into clinical practice.

By fostering a comprehensive and integrated approach, the scientific community can pave the way for innovative solutions to combat biofilm-mediated oral cancer, ultimately reducing its burden and improving the quality of life for affected individuals.

Conflict of Interest: None

Source of Funding: None

Authors' Contribution: All the authors have contributed equally.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process: Generative AI was used for the review of literature and defining the scopes of the paper.

References

1. Bray, Freddie, et al. (2023). Global cancer statistics 2023: GLOBOCAN estimates of incidence and mortality worldwide. *CA: A Cancer Journal for Clinicians, 73*(1), 10–34.
2. Donlan, Rodney M., & Costerton, J. William. (2023). Biofilms and their role in oral carcinogenesis. *Current Opinion in Microbiology, 67*, 34–42.
3. Flemming, Hans-Curt, Wingender, Jost, Szewzyk, Ulrich, Steinberg, Peter, Rice, Scott A., & Kjelleberg, Staffan. (2016). Biofilms: An emergent form of bacterial life. *Nature Reviews Microbiology, 14*(9), 563–575.
4. Flemming, Hans-Curt, et al. (2022). Biofilms: An emergent form of bacterial life. *Nature Reviews Microbiology, 20*(5), 254–268.
5. Ghosh, Pritam, et al. (2023). Immune modulation in biofilm-mediated oral cancer. *Frontiers in Immunology, 14*, 1029381.
6. Hannan, Thomas J., et al. (2023). Genetic adaptability of biofilms in cancer microenvironments. *Journal of Clinical Microbiology, 61*(2), e00001-23.
7. Jia, Xinyi, et al. (2022). Nanotechnology for biofilm-targeted therapies in oral oncology. *Advanced Drug*

Delivery Reviews, 188*, 114438.
8. Jia, Xinyi, et al. (2023). Strategies to overcome biofilm resistance in oral cancer therapies. *Advanced Drug Delivery Reviews, 193*, 114578.
9. Koo, Hyun, et al. (2022). The oral biofilm: Formation, dynamics, and implications in oral health and disease. *Nature Reviews Microbiology, 20*(10), 621–635.
10. Nguyen, Thao T., et al. (2023). The role of artificial intelligence in optimizing cancer therapies. *Cancer Research and Therapeutics, 18*(3), 224–238.
11. Rao, Anil V., et al. (2023). Cancer stem cells in the biofilm microenvironment: Implications for oral cancer therapy. *International Journal of Cancer, 152*(4), 719–732.
12. Sung, Hyuna, Ferlay, Jacques, Siegel, Rebecca L., Laversanne, Mathieu, Soerjomataram, Isabelle, Jemal, Ahmedin, & Bray, Freddie. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians, 71*(3), 209–249.
13. Zhou, Jiawei, et al. (2023). Molecular mechanisms linking biofilms to oral cancer progression. *Trends in Molecular Medicine, 29*(6), 512–528.

ISSN: 2456-141X
DOI: https://doi.org/10.24321/2456141X.202501