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Original Article

Advancing Oral Health: Preclinical Findings and Future Prospects of mRNA Vaccines in Dental Applications—A Comprehensive Review

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ABSTRACT

The rapid progress in mRNA vaccine technology, accelerated by the global COVID-19 crisis, has sparked growing interest in their use for conditions beyond infectious diseases. Dentistry has become an emerging area for exploring mRNA-based therapeutic approaches aimed at preventing and managing oral pathologies. This narrative review assesses the present landscape of mRNA vaccine research and its experimental use in oral health, particularly in relation to periodontal disorders, dental caries, regenerative strategies, implantology, and oral malignancies. Evidence was gathered from preclinical investigations—both in vitro and in animal models—to evaluate the capacity of mRNA-based interventions to influence immune mechanisms and promote repair within oral tissues. Clinical investigations were referenced only when relevant to broader applications of mRNA vaccines, such as in oncology and immune-based therapies. Preclinical evidence demonstrates that mRNA formulations can strengthen immune responses and support tissue-healing mechanisms. Nonetheless, their successful delivery in the intricate oral microenvironment remains a major obstacle. Issues such as maintaining vaccine integrity, optimizing delivery systems, and fine-tuning immune modulation still need to be addressed. Although mRNA vaccines show considerable promise for transforming dental therapeutics, substantial barriers concerning safety, efficacy, and clinical practicality persist. Continued research is crucial to overcome these limitations and facilitate their safe and effective integration into dental practice.

Keywords: mRNA vaccines, Oral health, Dentistry, Periodontal disease, Dental caries, Immune modulation, Regenerative medicine, Implantology

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Introduction

The remarkable success of mRNA vaccines during the COVID-19 pandemic has confirmed their powerful biological potential [1]. Yet, their relevance extends far beyond infectious disease control and epidemiology [2]. These vaccines influence the complex immune pathways involved in various diseases, demonstrating anti-inflammatory, immunomodulatory, antitumor, and regenerative functions [3-5] **(Figure 1)**. Despite these advances, their role in dentistry is still emerging [6]. Investigations have mainly explored how mRNA-based approaches might address frequent dental problems, including periodontal inflammation [7], implant integration [8], dental decay [9], and oral neoplasms [10]. However, much remains unknown about how these vaccines can be tailored to the specialized conditions within the oral cavity [11]. Major challenges include managing microbial ecosystems, reducing potential immune-related side effects, ensuring long-term biosafety, and tackling economic factors that influence accessibility. Moreover, refining delivery strategies and improving local immune modulation for effective regeneration are vital [12]. This review critically examines preclinical research on mRNA vaccines within the context of dentistry to evaluate their transformative potential for oral health care [13]. By compiling and analyzing current findings, the study identifies existing gaps and suggests directions for future inquiry [14]. Ultimately, the goal is to advance mRNA vaccines as viable therapeutic tools in dental medicine, addressing both opportunities and obstacles in this innovative field [15].

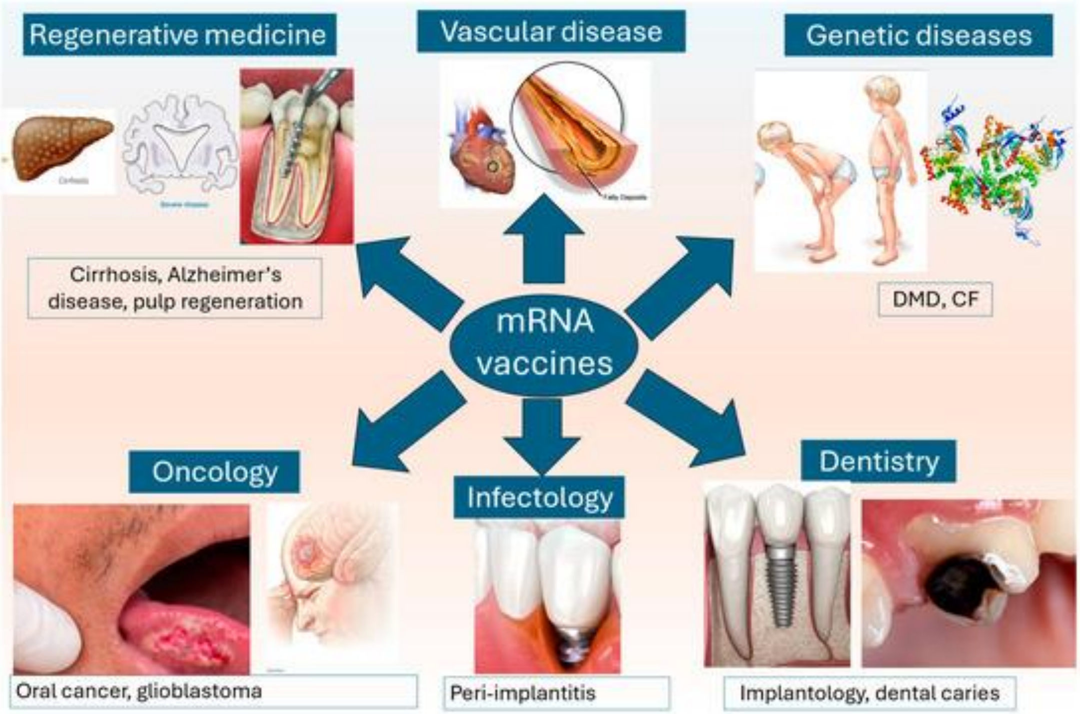

Figure 1. Potential applications of mRNA vaccines across medical disciplines due to their anti-inflammatory, immunomodulatory, antitumor, and regenerative properties

Basic Principles

mRNA vaccines in Dentistry: Overview and potential

The development, manufacturing, and biomedical application of mRNA vaccines are progressing at an exceptional rate, driven by encouraging data from numerous preclinical investigations spanning multiple medical domains [16-19]. mRNA therapeutics are increasingly recognized as versatile candidates for conditions imposing significant health and financial burdens, including cancer, heart failure, autoimmune disorders [20], and rare hereditary diseases [21]. Their appeal lies in their adaptability, cost-effectiveness, and relatively simple production, alongside fewer complications during administration [22]. Delivery typically involves nanoparticle carriers that safeguard the mRNA from degradation and facilitate its entry into the cytoplasm. Since translation occurs exclusively in the cytoplasm, there is no risk of genomic integration, and the absence of viral vectors minimizes the chance of insertional mutagenesis or autoimmune events [23]. While these technological breakthroughs are promising, dental applications of mRNA vaccines remain at an early stage yet hold substantial potential [24]. This technology provides a novel opportunity to tackle oral conditions such as periodontal disease, dental caries, and oral cancers—ailments that have historically posed treatment difficulties [25]. A distinct advantage of mRNA vaccines lies in their dual capability to modulate immune activity and stimulate tissue renewal [26]. For example, in oral lichen planus (OLP), mRNA constructs encoding immunoregulatory cytokines like interleukin-10 (IL-10) and transforming growth factor-beta (TGF-β) could help control T-cell–mediated responses, thereby reducing inflammation. Meanwhile, mRNA encoding growth-promoting factors such as epidermal growth factor (EGF) and fibroblast growth factor (FGF) could enhance cell proliferation and repair processes within damaged oral mucosa [27].

Obstacles to delivering mRNA vaccines in dental applications

Although mRNA vaccines demonstrate great potential, a number of barriers still hinder their adaptation to dental medicine. One of the most critical issues involves maintaining mRNA integrity in the highly variable oral setting [28]. Constant exposure to saliva, fluctuating acidity, and a dense microbial population make it difficult for mRNA to remain stable for long periods [29]. Therefore, developing delivery platforms capable of directing mRNA precisely to oral tissues is essential for achieving successful outcomes [30]. Another important factor is maintaining immune equilibrium—stimulating defense mechanisms without provoking excessive inflammation that could worsen existing conditions [31]. Experimental research confirms that mRNA vaccines can influence immune regulation and encourage tissue regeneration, yet translating these findings into clinical dentistry remains an ongoing challenge [32]. Future investigations should prioritize the identification of oral-specific antigens and the creation of delivery systems uniquely adapted to the oral cavity to maximize vaccine performance in this area [33].

Potential risks, ethical issues, and future outlook

As an emerging therapeutic approach, mRNA vaccines in dental science must undergo comprehensive risk evaluation. Despite their success in other medical fields, localized inflammation and unpredictable immune activation remain major concerns when used within oral tissues [34]. Extensive testing—both through preclinical experiments in vitro and in animal models, as well as in human trials—will be necessary to establish their reliability and clinical safety [35]. Ethical topics also warrant careful discussion, including the protection of patient welfare, fairness in access to new treatment technologies, and the responsible use of regenerative approaches for non-essential aesthetic procedures [36]. As this research area matures, ensuring both safety and efficacy will be vital to enable mRNA vaccines to transition from the laboratory to standard dental practice [37].

Head and Neck Cancer

mRNA-Based strategies for HPV-associated head and neck tumors

In the last few years, RNA vaccines have gained notable attention for their role in combating head and neck cancers, particularly those linked to human papillomavirus (HPV) infections [38]. Multiple mRNA configurations—such as self-amplifying constructs, unmodified non-replicating sequences, and nucleoside-modified non-replicating versions—are currently under evaluation in preclinical settings [39]. These formulations code for tumor-associated proteins like Gde7, provoking immune recognition of cancer-specific antigens [40] **(Figure 2)**. Stimulating CD8$^+$ T-cell activity has proven especially promising in halting tumor development, with stronger results than previous DNA-based Gde7 vaccines [41]. Nonetheless, as is common in cancer immunotherapy, initial preclinical success often faces difficulties with reproducibility and consistent efficacy across experimental systems [42].

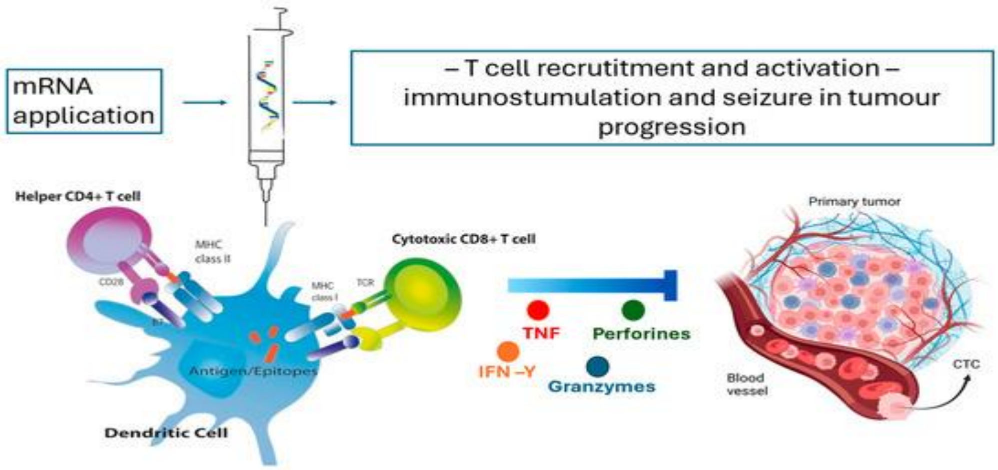

Figure 2. Overview of how mRNA vaccines may shape the future of immunotherapy and personalized oncology. Once introduced, mRNA molecules are translated into proteins displayed on antigen-presenting cells (APCs) through MHC I and II pathways. Engagement of CD28 and TCR then triggers CD4$^+$ and CD8$^+$ T-cell activation, leading to an amplified immune response that slows tumor growth

Two major strategies dominate mRNA vaccine delivery in current studies: direct injection and ex vivo dendritic cell (DC) loading [43]. Direct administration is quicker and less expensive but poses challenges due to the enzymatic breakdown of RNA by natural RNases in the body [44]. Encapsulation in lipid nanoparticles (LNPs) or positively charged complexes can help preserve mRNA integrity, enhance cellular absorption, and boost immune activation [45, 46]. In contrast, ex vivo DC-based vaccination allows for refined control of antigen presentation and can produce stronger immune responses, though it remains time-intensive, technically demanding, and expensive because of the need to isolate, modify, and reinfuse DCs.

Broadening the use of mRNA vaccines for Non-HPV head and neck tumors

While lipid nanoparticles (LNPs) have significantly improved mRNA protection and uptake, they also introduce complications such as toxicity risks, unwanted immune reactions, and targeting difficulties [47]. These drawbacks, shared by many nanoparticle-driven delivery systems, underscore the importance of refining such approaches for application in head and neck oncology [48]. Achieving a balance between strong therapeutic impact and biological safety will be key, necessitating additional in-depth research [49].

Although most available data emphasize HPV-related tumors, expanding mRNA technology to non-HPV-associated cancers represents a major future opportunity [50]. Promising immune activation observed in murine studies requires further exploration to assess its duration, magnitude, and overall effectiveness [51]. Long-term investigations will be essential to validate these preclinical results and define their clinical importance [52]. In summary, mRNA vaccine strategies hold great promise for treating head and neck cancers, particularly HPV-driven cases [53]. However, advancing delivery techniques, improving immune monitoring, and expanding research into non-HPV cancers are crucial steps toward clinical translation and therapeutic application.

Regenerative Medicine

mRNA vaccines in regenerative Medicine: Mechanisms and approaches

Messenger RNA (mRNA) technologies have recently gained momentum in regenerative medicine for their capacity to encode bioactive molecules capable of inducing cellular transformation and differentiation [54]. Unlike conventional gene therapy, mRNA platforms avoid genomic integration, providing a much safer profile that has intensified research attention [55]. Two principal strategies have evolved for regenerative purposes: the use of mRNA to drive the differentiation of induced pluripotent stem cells (iPSCs) and the direct conversion of somatic cells into specialized types [56]. In the iPSC-based method, adult cells are reprogrammed into a pluripotent state and then guided toward particular functional lineages. Although efficient, this process can result in tumor formation if undifferentiated cells persist [57]. In contrast, direct reprogramming eliminates the pluripotent step by converting mature cells straight into specific cell types. This approach offers a reduced oncogenic risk but still struggles with yield and clinical scalability [58] **(Figure 3)**. Across medicine, mRNA treatments have proven versatile in promoting tissue recovery—for example, VEGF-A mRNA has aided cardiac regeneration, and dystrophin-directed therapies have shown potential in repairing muscle damage in Duchenne muscular dystrophy [59, 60].

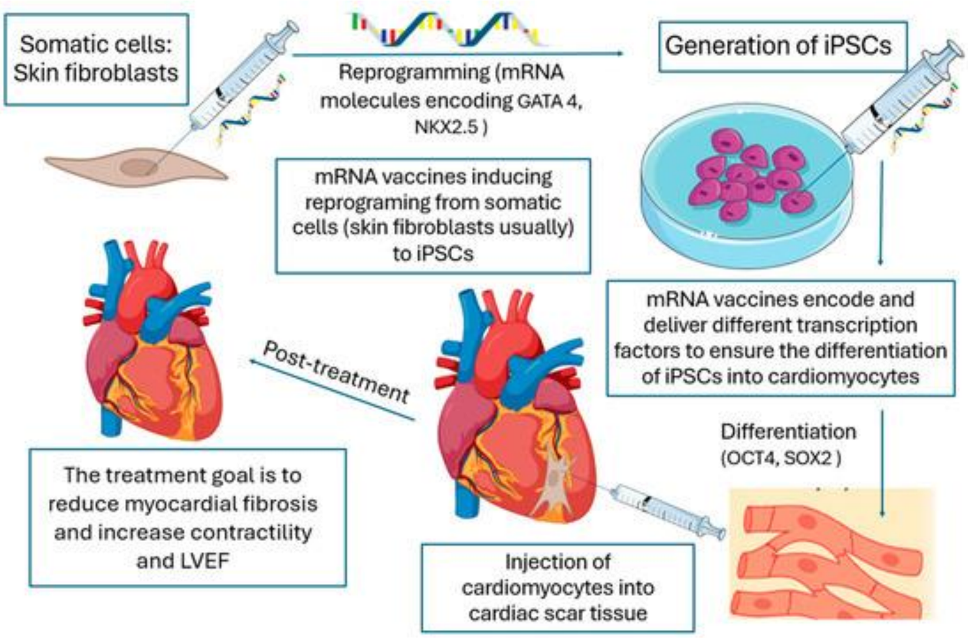

Figure 3. The underlying concepts of mRNA-driven tissue repair are broadly similar across medical disciplines. In cardiac fibrosis models, mRNA administration initiates pluripotency, cellular reprogramming, and differentiation, restoring functional cardiomyocytes and improving cardiac contractility along with left ventricular ejection fraction (LVEF). The central goal is to regenerate functional parenchymal tissue. Key transcriptional regulators—OCT4 and SOX2 for differentiation, and GATA4 and NKX2.5 for

reprogramming—are typically delivered through mRNA constructs to achieve this outcome

mRNA-Based regenerative therapies in dentistry: Opportunities and challenges

In dental research, mRNA-based regenerative strategies have shown notable potential in bone reconstruction and implantology. In a study by Itaka *et al.*, mRNA encoding the osteogenic regulator Runx2 and the angiogenic factor VEGF acted synergistically to accelerate jawbone restoration in rat models [61]. Runx2 promoted osteoblast differentiation, while VEGF enhanced new vessel growth, together creating a favorable environment for bone formation. Expression of osteogenic markers such as osteopontin and osteocalcin increased substantially, confirming enhanced bone metabolism [62, 63]. Parallel investigations by Zhang *et al.* and Xu Q *et al.* validated these interactions, emphasizing the joint impact of Runx2 and VEGF in supporting optimal bone healing [64, 65]. However, Zhang *et al.*'s (2023) work involved only a limited sample of 30 rats, restricting the clinical implications [66]. Larger animal trials are therefore necessary before progressing toward human applications.

Further innovation in delivery technologies—especially in lipid nanoparticle (LNP) formulations—is essential to refine stability, boost transfection efficiency, and minimize immune activation [67]. Transitioning mRNA-based regenerative therapy into clinical dentistry will also depend on navigating ethical and regulatory challenges, ensuring biosafety, managing immunogenicity, and reducing economic inequities [68]. Ultimately, collaborative efforts among multiple scientific and clinical disciplines will be vital for overcoming current limitations and realizing the full therapeutic scope of mRNA technology in tissue regeneration.

Implantology

The promise of mRNA vaccines in dental implantology

mRNA-based interventions are emerging as a powerful tool in dental implantology, offering the possibility to enhance healing and improve patient recovery through precise modulation of molecular and immune pathways. These therapeutic effects, initially demonstrated in orthopedic joint implants, can potentially accelerate tissue regeneration around dental implants [69]. Translating these orthopedic outcomes to the oral environment, however, requires careful adaptation due to challenges such as the diversity of oral microbiota and variations in alveolar bone quality [70].

These vaccines can help control postoperative inflammation by fine-tuning immune responses and encouraging the release of anti-inflammatory cytokines, which prevents excessive immune activation at the site of implantation [71]. Local VEGF expression supports new blood vessel formation, providing necessary nutrients, while bone morphogenetic proteins (BMPs), particularly BMP-2, stimulate osteoblast differentiation and mineral deposition to accelerate bone repair [72]. Together, these mechanisms promote osseointegration—the formation of new bone around the implant—enhancing stability, reducing infection risk, and lowering the likelihood of implant failure [73]. The combination of immunomodulatory, anti-inflammatory, and regenerative effects positions mRNA therapies as a groundbreaking approach in dental implantology [74].

Research progress and challenges in mRNA dental applications

Several preclinical studies provide evidence for the potential of mRNA vaccines in improving dental implant outcomes. Liu *et al.* reported that BMP-2 mRNA improved osteogenic activity in periodontal ligament stem cells, suggesting enhanced integration of implants [75]. Similarly, Zhou *et al.* demonstrated accelerated bone regeneration and improved implant fixation in rats treated with BMP-2 mRNA following implant failure [76]. These findings indicate that mRNA-based treatments could be particularly valuable for patients with poor bone quality or delayed healing.

Despite promising results, obstacles remain. Immune overactivation is a significant concern, as excessive inflammation can compromise bone healing [77]. The oral cavity presents additional challenges, such as fluctuating temperature and moisture, which can affect mRNA stability. Lipid nanoparticles (LNPs) are commonly used to protect and deliver mRNA, but their design needs refinement for oral applications. Optimal LNPs should have diameters between 50–150 nm to maximize cellular uptake while avoiding clearance by the body's reticuloendothelial system. Modifying lipid composition—through ionizable and PEGylated lipids—can further improve stability and ensure controlled mRNA release directly to bone or surrounding tissues [78].

Future directions and clinical translation

mRNA vaccines have the potential to transform dental implantology by promoting more efficient osseointegration and tissue repair [79]. Nevertheless, applying orthopedic findings to dental practice requires addressing unique oral factors, including interactions with oral microbes and compatibility with dental materials [80]. Future studies should focus on refining delivery systems, optimizing formulations, and evaluating long-term safety and efficacy. Cost-effectiveness is also an important consideration, as localized mRNA interventions could impose financial barriers [81].

Dental caries

Pathogenesis overview

Dental caries is a chronic, multifactorial disease primarily driven by biofilm formation, with Streptococcus mutans identified as the main causative organism due to its superior ability to form structured biofilms [82]. Within the plaque matrix, S. mutans metabolizes polysaccharides to produce lactic acid, accounting for approximately 70% of the total organic acids in the biofilm [83]. This acid accumulation disrupts the natural balance between demineralization and remineralization of enamel, favoring tooth decay [84] **(Figure 4)**. Consequently, strategies aimed at preventing biofilm formation represent promising approaches for caries prevention [85].

Potential of RNA-Based therapies in caries prevention

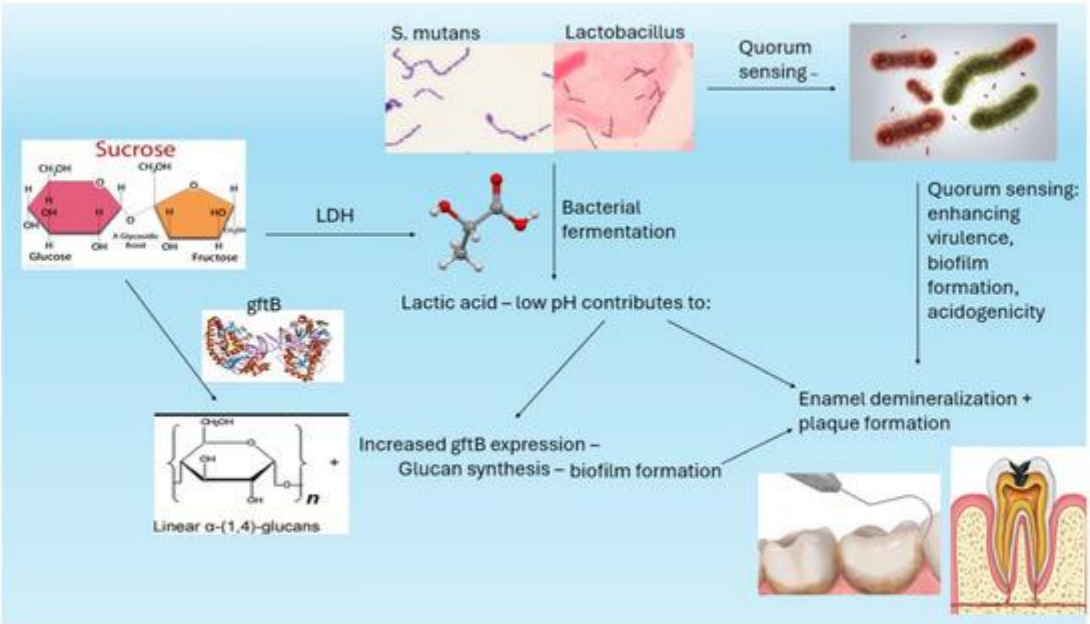

Figure 4. The pathogenesis of dental caries highlights potential intervention points for mRNA vaccines. Targeting S. mutans could inhibit the synthesis of glucan-based polysaccharides and reduce lactic acid production, thereby limiting demineralization and plaque accumulation. Other bacterial species, such as Lactobacillus, contribute to biofilm development and communicate through quorum-sensing pathways, which may also serve as potential targets for RNA-based preventive strategies

In modern dentistry, there has been a shift towards prioritizing disease prevention and maintaining tooth integrity over surgical treatments [86]. One of the early advancements, in 2006, involved the creation of oligodeoxyribonucleotides designed to target gtfB mRNA. This approach helped to decrease glucan production and inhibit biofilm formation [87]. However, RNA-based treatments saw limited progress until more recent innovations. In 2024, a revolutionary method developed by Shung Yu combined antisense vicK RNA (ASvicK) from S. mutans with Dimethylaminohexadecyl methacrylate (DMAHDM), demonstrating a powerful synergy in reducing biofilm formation. ASvicK specifically targets and suppresses the expression of the vicK gene, which is vital for glucan production, thereby destabilizing the biofilm and diminishing its pathogenic potential [88]. On the other hand, DMAHDM interacts with bacterial cell membranes, embedding itself into the lipid layers, disrupting their integrity, and promoting cell death. This dual approach proves far more effective in reducing biofilm growth and the risk of cavities compared to single-target methods. Laboratory tests confirm that this combination also helps reduce enamel demineralization, showing promise in the prevention of early-stage caries. Overall, this novel treatment addresses key stages of dental caries development, offering a promising preventive approach via RNA technology.

The future of mRNA vaccines for dental caries

Previously believed to be an issue limited to children, dental caries has now been recognized as a disease that continues to affect adults, with prevalence rates ranging from 26% to 85% [89]. While the initial costs of developing and administering anti-caries vaccines are high, these vaccines could lead to substantial cost savings in the long run. Traditional preventive methods, like using fluoride toothpaste and scheduling regular dentist visits, demand constant effort and ongoing maintenance [90]. Conversely, an anti-caries vaccine could provide lasting immunity against Streptococcus mutans, significantly reducing the need for recurring treatments, such as fillings and root canals, and decreasing the risk of complications like infective endocarditis and bone deterioration [91]. This move from treatment-focused to prevention-based care has the potential to revolutionize oral health by providing a sustainable, proactive solution [92].

The application of mRNA vaccines in fighting dental caries is especially promising. New therapies, such as combining ASvicK RNA and DMAHDM, have proven effective in lab studies by targeting bacterial virulence and metabolism [93]. These innovations demonstrate the potential for mRNA vaccines to alleviate the global impact of caries [94]. However, clinical trials are still in their infancy, and obstacles such as research funding, high costs, and regulatory approvals need to be addressed. Additional challenges include public hesitancy, difficulties in administering the vaccine in dental settings, and concerns about antimicrobial resistance. Overcoming these hurdles and advancing research into clinical practice will be crucial for broad implementation [95]. If successfully developed, anti-caries vaccines could dramatically improve long-term oral health, reduce treatment costs, and enhance quality of life.

Periodontal Disease

Understanding the pathogenesis of periodontal disease

Periodontal disease (PD) is a persistent inflammatory condition caused by an imbalance in oral microbiota, characterized by the destruction of tissues supporting the teeth. The progression of PD does not rely solely on P. gingivalis, but instead is influenced by its interactions with other pathogens like F. nucleatum, which helps stabilize biofilms and amplifies P. gingivalis' pathogenic effects. Other significant microorganisms involved in PD include Aggregatibacter actinomycetemcomitans, Fusobacterium nucleatum, and Eikenella corrodens [96]. These pathogens interfere with the host's immune system by disrupting the activity of Toll-like receptors and complement pathways, undermining neutrophil and macrophage function. This leads to an imbalance in the microbial community, immune system malfunction, excessive inflammation, and the breakdown of bone tissue through processes like matrix metalloproteinase release, RANKL production, reactive oxygen species (ROS) generation, and tissue necrosis [97]. Despite numerous treatment approaches, no single therapy has proven to be universally successful. Since inflammation is a major factor in disease development, certain progress has been made using anti-TNF-α and anti-IL-1 treatments [98]. However, because P. gingivalis and dysbiosis are key drivers of tissue damage, the most logical strategy may involve early vaccination to prevent bacterial colonization and the onset of subsequent pathological events in the mouth [99].

Impact of immune system disruption

Research suggests that variation in bacterial strains might explain the diverse progression of diseases, as less virulent strains tend to coexist in asymptomatic individuals [100]. Furthermore, immune system malfunctions play a crucial role in advancing the disease, with persistent inflammation primarily caused by imbalanced T-helper cell activity (Th1 and Th17) and insufficient functioning of regulatory T-cells (Tregs) [101]. For example, Vaernewyck *et al.* highlighted an overly activated mucosal immune response. However, the observed variability in immune reactions based on bacterial strains underscores the importance of focused research to enhance vaccine targeting and immune regulation [102]. These findings emphasize the need to consider both microbial behavior and immune dysfunction to fully understand the progression of periodontal disease (PD).

Host factors influencing disease development

Factors intrinsic to the host, such as immune function, genetic makeup, and environmental exposures, significantly influence the course of PD [103]. The inability to properly regulate immune responses, leading to persistent inflammation, is a key contributor to tissue damage [104]. Salivary secretory IgA (SIgA) has emerged as an important protective agent that helps maintain a balanced relationship between the host and the microbiome [105]. However, systemic conditions, like diabetes, or lifestyle choices, such as smoking, can disrupt this balance, making the disease more severe. This highlights the need for research that investigates the interaction between host factors and microbial influences to design tailored prevention and treatment strategies.

mRNA vaccines: A new frontier for pd prevention

mRNA vaccines offer an innovative strategy for preventing PD by focusing on key pathogens and modulating immune responses. These vaccines introduce antigens designed to trigger protective immunity, with the goal of halting biofilm formation and mitigating inflammation-related tissue damage. Studies in animal models, especially rodents, have shown that mRNA vaccines targeting *P. gingivalis* can reduce alveolar bone resorption and inflammation by stimulating a strong SIgA response. Mucosal vaccines, in particular, have demonstrated superior efficacy compared to systemic approaches, providing robust immunity in the oral cavity. Despite this, challenges remain in optimizing the balance between vaccine-induced immunity and inflammation control. Lipid nanoparticles (LNPs) have enhanced antigen expression but have also been linked to excessive cytokine release. Modifying the mRNA sequence, similar to the approaches used in COVID-19 vaccines, could improve immune response while reducing inflammatory side effects [106].

Overcoming obstacles in vaccine development

Although preclinical studies are promising, there are still many challenges to making mRNA vaccines for PD viable in clinical practice. PD's complex, polymicrobial nature requires vaccines capable of targeting multiple pathogens to address dysbiosis effectively [107]. Results from trials in larger animal models, such as dogs, have been inconsistent, likely due to species-specific differences in microbiota composition and the complexity of PD pathogenesis [108]. Future studies should aim to better align vaccine formulations with human disease mechanisms [109]. Optimizing mucosal vaccination is especially important, as it has been shown to generate stronger immune responses, particularly IgA. Further work is needed to explore how host susceptibility and environmental factors can be integrated into vaccine designs to ensure they are broadly effective. While the complexity of PD presents challenges, combining multivalent vaccines with mucosal delivery could be a promising route for effective prevention and management [110-112]. One key issue for RNA-based vaccines in periodontitis is achieving a strong immune response without exacerbating inflammation, which is a core feature of the disease [113]. Therefore, optimizing formulations to boost immunity while avoiding inflammation-driven damage is critical for success [114].

Conclusion

To sum up, while mRNA vaccines hold great potential in the field of dentistry, especially for conditions like dental caries, periodontal disease, and implantology, their clinical application is still in its infancy. Further research is necessary to address crucial challenges, such as enhancing vaccine formulations for localized use, ensuring efficient delivery systems, and preventing adverse immune reactions [115]. Additionally, the transition from preclinical studies to human trials faces numerous regulatory and acceptance challenges. While mRNA vaccines have proven successful in other medical domains, future research must focus on their specific applications in dental care to ensure that benefits outweigh the risks [116]. In the long term, mRNA vaccines could fundamentally change dental practices by improving immune defenses, preventing infections, and promoting tissue regeneration. However, a thorough understanding of their safety, effectiveness, and long-term outcomes will be essential for their successful integration into clinical settings [117].

Table 1. This table outlines the various applications of mRNA technology within dentistry, focusing on areas like regenerative therapies, cancer treatments, and combating infectious or inflammatory conditions. Examples include the use of mRNA to produce BMP-2 for tissue repair, mRNA-based vaccines targeting HPV-related cancers, antisense oligonucleotides to mitigate bacterial virulence in dental caries, and approaches for modulating immune responses in periodontal disease. It also addresses the difficulties in enhancing lipid nanoparticle (LNP) delivery systems for mRNA, underscoring the necessity for continued research to fully harness the therapeutic benefits of mRNA technologies in oral health care

Application Domain	Research Focus	Investigators/Source	Study Nature	Core Observations	Supplementary Notes
Bone and Tissue Restoration	mRNA-Induced BMP-2 Promotes Bone Growth in Periodontal Stem Cells	Liu *et al.* 75]	Preclinical/Cell-Based	BMP-2 mRNA enhanced bone formation in periodontal ligament stem cells.	Holds promise for regenerating dental tissues.
	BMP-2 mRNA Speeds Up Recovery and	Zhou *et al.* [76]	Preclinical/Animal Testing	BMP-2 mRNA accelerated healing	Highlights bone-

	Stabilizes Implants in Rat Models			and improved implant stability in rats with dental implant failures.	stimulating capabilities of mRNA in living systems.
HPV-Linked Head and Neck Tumors	BNT113 with Pembrolizumab for Initial Treatment of Advanced HNSCC: Early Safety Insights	Klinghammer *et al.* [53]	Human Trial	Initial safety results showed positive outcomes from combining BNT113 mRNA vaccine with pembrolizumab for advanced, unresectable HNSCC.	BNT113 targets HPV-16 E6 and E7 antigens associated with HPV-driven head and neck cancers.
Non-HPV Oral Tumors	Custom mRNA Vaccines Paired with Immune Modulators for Oral Tumor Therapy	Gheena and Ezhilarasan [16]	Preclinical	Custom mRNA vaccines combined with immune modulators improved tumor immunity and patient outcomes in oral tumor models.	Emphasizes the combined effect of mRNA vaccines and immune modulators in oral tumor treatment.
Dental Decay	Antisense Oligodeoxyribonucleotides Targeting gtfB mRNA Suppress Streptococcus mutans Activity	Guo *et al.* [87]	Preclinical	Antisense oligodeoxyribonucleotides targeting gtfB mRNA reduced gtfB expression and function in Streptococcus mutans.	Focuses on disrupting bacterial genes to lower caries-causing activity.
	ASvicK RNA with DMAHDM Reduces Biofilm and Protects Enamel	Shung Yu [89]	Preclinical/Cell-Based	ASvicK RNA combined with DMAHDM inhibited biofilm growth and enamel erosion.	Suggests RNA-based strategies for preventing dental decay.
Gum Inflammation	Suppressing Th17 Cells: A Novel Strategy for Oral Mucosal Inflammation	Wang *et al.* [100]	Preclinical	Reducing Th17 cell activity decreased inflammation in oral mucosal conditions, including gum inflammation, by regulating immune responses.	Offers a potential approach for managing oral mucosal inflammatory conditions.
	Oral Mucosal Immunization Against Gum Inflammation: Current Advances and Potential	Vaernewyck [102]	Preclinical	Oral mucosal vaccines elicited strong salivary IgA responses.	Indicates effectiveness of mRNA-based mucosal vaccines in the oral environment.
Delivery Optimization	Enhancing mRNA Lipid Nanoparticle Systems: Delivery and Therapeutic Insights	Liu *et al.* [117]	Preclinical/Cell-Based	Particle size, surface charge, and ionizable lipids are critical for effective and stable mRNA delivery.	Provides guidance on improving lipid nanoparticle systems for mRNA applications.

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Ethics Statement: None

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