Epigenetic modifications as a biomarker for periodontitis and peri-implantitis: a review

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Abstract

The study of epigenetics is critical for understanding the interplay between genetic susceptibility and environmental influences in diseases like periodontitis and peri-implantitis. Epigenetic modifications—including DNA methylation, histone modifications, and non-coding RNA activity—can alter gene expression without changing the DNA structure, thereby impacting disease progression and tissue destruction. This review brings updated and straightforward information on the role of epigenetics in the pathogenesis of periodontal and peri-implant diseases, highlighting the contributions of microbial factors, host immunity, and systemic conditions like diabetes. Recent advancements in genomic sciences, such as high-throughput sequencing and methylation profiling, have revealed specific patterns of DNA methylation and chromatin modifications that precede pathological states. These findings enhance our understanding of the molecular pathology of periodontal and peri-implant infections and suggest novel treatment approaches to reverse the epigenetic effects associated with disease progression. Histone modifications also play a significant role in regulating periodontal disease by altering DNA accessibility for gene transcription, affecting genes involved in immune response and inflammation. Non-coding RNAs, particularly microRNAs, have been identified as critical regulators of inflammatory pathways and potential therapeutic targets. The epigenetic landscape is further complicated by systemic diseases like diabetes, which can influence epigenetic modifications and exacerbate periodontal inflammation and tissue destruction. Understanding these interactions is essential for developing comprehensive preventive protocols and therapeutic strategies. Epigenetic therapies, or "epidrugs", offer promising new treatment modalities by targeting specific epigenetic modifications to normalize gene function and facilitate tissue repair. However, a thorough understanding of epigenetic mapping in these diseases is required, necessitating further epidemiologic studies to identify the exact modifications involved. In conclusion, integrating epigenetic research into periodontology provides a promising approach better to understand gene-environment-microbiome interactions in periodontal and peri-implant diseases. This integration could lead to developing new therapies and preventive strategies, ultimately improving clinical outcomes for patients affected by these conditions.

Keywords: epigenetics, periodontitis, peri-implantitis, DNA, RNA, methylation, histones.

Introduction

The study of epigenetics is crucial for integrating an individual's genetic susceptibility to diseases, including periodontitis and peri-implantitis, with environmental influences.

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Even though the survival rate of dental implants is high [1-4], some new information has led investigators to understand better how to prevent or manage implant-related diseases [5-7]. some components of epigenetic modification—DNA methylation, histone modifications, and non-coding RNA activity—can modify gene expression without altering DNA structure. This regulation particularly benefits chronic inflammatory diseases, as host immunity contributes to disease progression and tissue destruction [8,9].

Relapse and remission cycles of periodontitis and peri-implantitis lead to inflammation, tissue destruction, and, if untreated, tooth or dental implant loss. Numerous factors contribute to these diseases, such as oral bacteria, host immunity, and systemic conditions like diabetes [9,10]. Research indicates that epigenetic modifications can reshape host reactions to these agents, including bacteria, thereby dictating the severity and nature of periodontal and peri-implant diseases [11-13].

For instance, hypermethylation of genes related to the inflammatory system is linked to chronic diseases like periodontitis and peri-implantitis, where epigenetic modifications serve as diagnostic biomarkers of disease severity (Fig. 1) [14,15]. This review aims to verify findings from the literature correlating epigenetics with periodontitis and peri-implantitis.

Literature review

Periodontitis refers to inflammation of the tissues surrounding the teeth [16], while peri-implantitis involves inflammation around dental implants, leading to bleeding, edema, bone resorption, and implant failure [17-19]. Both conditions are triggered by microbial factors [7] and host immune responses, potentially regulated through epigenetics [20,21].

The epigenetic process, particularly DNA methylation, plays a critical role in how genes respond to environmental stimuli, especially microbial load. DNA methylation can either repress or activate genes vital for immune response and inflammation. For example, hypermethylation of the TLR2 and TLR4 gene promoters is associated with a weakened immune response to periodontitis-causing microorganisms, exacerbating inflammation and tissue breakdown [14,22]. This suggests that epigenetic changes can serve as biomarkers for disease prognosis and progression.

Understanding epigenetic patterns in the pathogenesis of periodontitis and peri-implantitis can help identify preventive and therapeutic strategies. The relationship between epigenetics and these diseases is further complicated by systemic conditions like diabetes, which also influence epigenetic modifications [9,10]. For example, hyperglycemia alters DNA methylation in periodontal and peri-implant tissues, affecting inflammatory response and tissue remodeling [10].

Recent advances in genomic sciences have uncovered epigenetic changes involved in periodontal and peri-implant diseases. High-throughput sequencing and methylation profiling have revealed specific DNA methylation and chromatin modification patterns preceding pathological states [23,24]. These findings enhance our understanding of the molecular pathology of periodontal and peri-implant infections and suggest novel treatment approaches to reverse epigenetic effects associated with disease progression.

Developments in epigenetic therapies, or “epidrugs,”

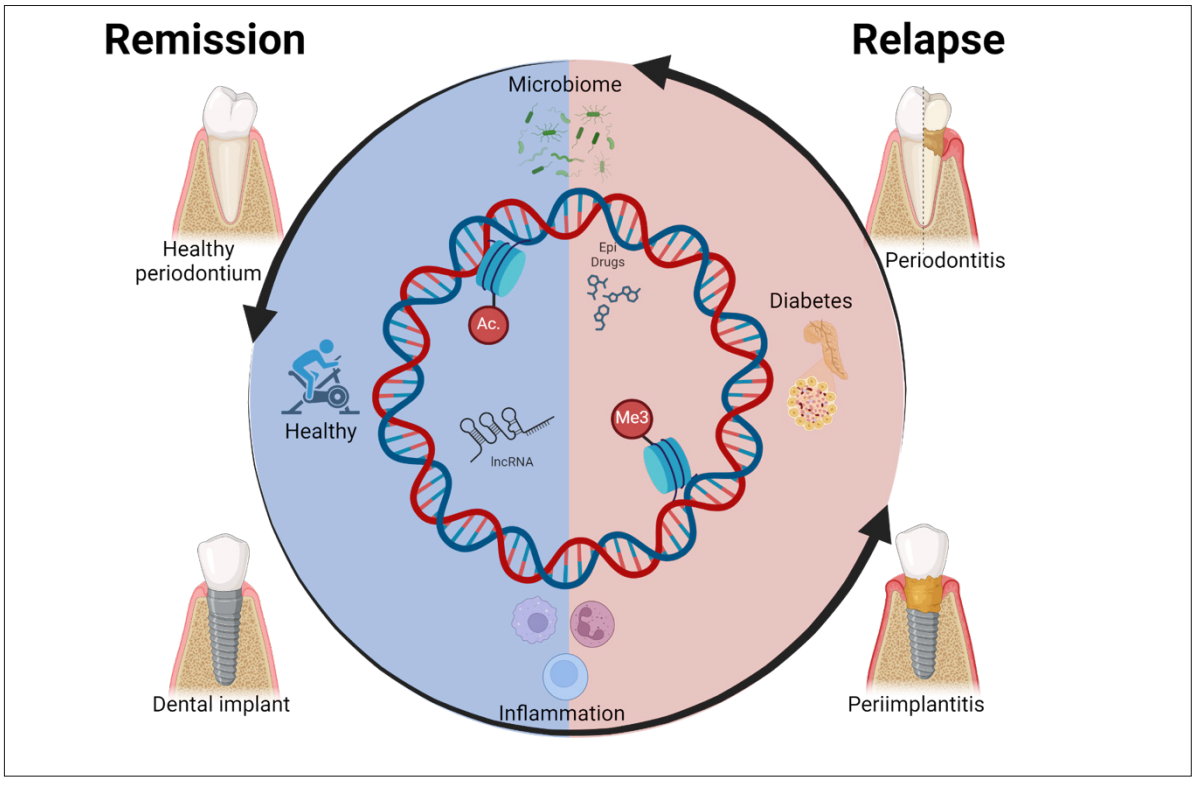

Figure 1. Relapse and remission of the periodontal diseases showing microbiological and epigenetic involvement.

offer potential clinical applications for regulating gene expression in periodontal and peri-implant tissues. Targeting specific epigenetic modifications could normalize gene function and facilitate tissue repair [25,26]. However, a comprehensive understanding of epigenetic mapping in these diseases is required, necessitating further epidemiologic studies to identify the exact modifications involved.

Histone modifications, such as acetylation and methylation, significantly contribute to the epigenetic regulation of periodontal disease by altering DNA accessibility for gene transcription. For instance, interleukin (IL)-8, an inflammation marker, is regulated by histone acetylation before bacterial infection, indicating that histone changes could manage periodontal inflammation [10,11].

Non-coding RNAs, especially microRNAs like miR-146a and miR-499, also play crucial roles in periodontal disease development by targeting critical inflammatory pathways [27,28]. Understanding the functions of these molecules could reveal new therapeutic targets.

Chronic inflammation creates stable DNA methylation patterns on genes involved in immune responses, altering the host's susceptibility to further infections. This highlights the importance of preventive protocols to arrest disease progression [9-11]. Epigenetic factors in peri-implantitis are similar to those in periodontal diseases, affecting implant success rates. Characterizing the epigenetic profile of peri-implantitis could provide insights into its etiology and aid in preventing implant complications [20,21].

Epigenetic therapies offer new treatment modalities for periodontal and peri-implant diseases by modulating gene expression and promoting tissue regeneration [27,28]. Integrating epigenetic research in periodontology [29] promises a better understanding of gene-environment-microbiome interactions and the development of new therapies to reduce disease risk.

Systemic diseases like diabetes also influence epigenetic modifications and exacerbate periodontal inflammation and tissue destruction. Controlling systemic diseases is thus essential in managing periodontal and peri-implant conditions [9,10,30]. A multi-faceted approach considering both local and systemic factors is recommended for managing periodontal diseases.

Conclusion

Epigenetic approaches hold the potential to elucidate periodontal and peri-implant diseases. By understanding how DNA methylation, histone modifications, and non-coding RNAs contribute to these conditions, researchers can discover new therapeutic targets and preventive strategies. The challenge lies in translating epigenomic discoveries into better clinical outcomes for patients with periodontal and peri-implant diseases.

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Conflicts of Interest

The authors declare no conflict of interest.

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