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Long non-coding RNAs as a therapeutic target for periodontitis

Periodontitis is a chronic inflammatory infectious disease characterized by the progressive destruction of the tissue supporting the teeth. It includes alveolar bone, cementum, gingiva, and periodontal ligament.[1] According to the Global Burden of Disease Study (2016) report, severe periodontitis is the 11th most prevalent condition in the world.[2] Several factors influence the risk of periodontal disease, and it can be reversible when given proper treatments. However, the reconstruction of destructive periodontal tissue is made possible by our human periodontal ligament (PDL) tissues and periodontal ligament stem cells (PDLSCs). Periodontal ligament cells have a regenerative property, and PDLSCs play a crucial role in osteogenic differentiation. The primary function of PDL is to keep the teeth in place, but it also helps to maintain tissue homeostasis and rebuild damaged periodontal tissues.[3]

Long non-coding RNAs (lncRNAs) do not encode proteins but play various roles in the regulatory process and pathogenesis of numerous diseases. LncRNAs regulate several gene expressions at various transcriptional and post-transcriptional levels. The functional mechanisms of lncRNAs are very diverse; they act as coactivators of transcriptional factors, which modulate several genes' expression in diverse cell types. lncRNAs interact with various cellular molecules, which include DNA, RNA, proteins, and metal ions. Between RNA and lncRNA interactions are crucial roles like mRNA splicing and modulation of subcellular dispersal and turnover.

In the *in vitro* study of healthy PDLSCs and infectious PDLSCs, the antisense non-coding RNA in the INK4 locus (ANRIL) lncRNA expression level is significantly decreased, while miR-7-5p expression was increased in infectious PDLSCs compared to healthy PDLSCs. This indicates that infectious PDLSCs had lower osteogenic activity when compared to healthy PDLSCs. ANRIL might play a positive role in the potential differentiation of osteogenic. High expression of ANRIL promotes osteogenic differentiation in infectious PDLSCs by upregulating alkaline phosphatase (ALP), osterix (OSX), and Runt-related transcription factor-2 (RUNX2) proteins. It's confirmed by western blotting analysis. The ANRIL lncRNA promotes bone formation by regulating miR-7-5p/IGF-1R.[4]

Interestingly, the lncRNAs act as competing endogenous RNAs (ceRNAs) known as miRNA sponges, that are competitively binding to miRNAs for protecting them from degradation. The ceRNA networks on the pathogenesis of the periodontal disease involve three lncRNA such as FGD5 Antisense RNA 1 (FGD5-AS1), Metastasis Associated Lung Adenocarcinoma Transcript 1 (MALAT1), and Taurine Up-Regulated 1 (TUG1).[5] Thus, the long noncoding RNAs play a critical regulatory role in the pathogenesis of the periodontal disease. The binding of lncRNAs and miRNA causes differential expression of miRNA, which leads to dysregulated expression and inhibition of several proteins. Those proteins are playing a crucial role in osteogenic differentiation, PDLSCs proliferation, and inflammation in periodontal infection [Fig. 1].

The role of lncRNA plays a critical regulatory process in periodontitis; they might be a turning point for other periodontal infection factors to lead to the disease. The lncRNAs might be helpful as a therapeutic target for the treatment of periodontitis. Further studies in periodontal and lncRNAs with experimental animal model studies will be helpful in better treatment for periodontitis.

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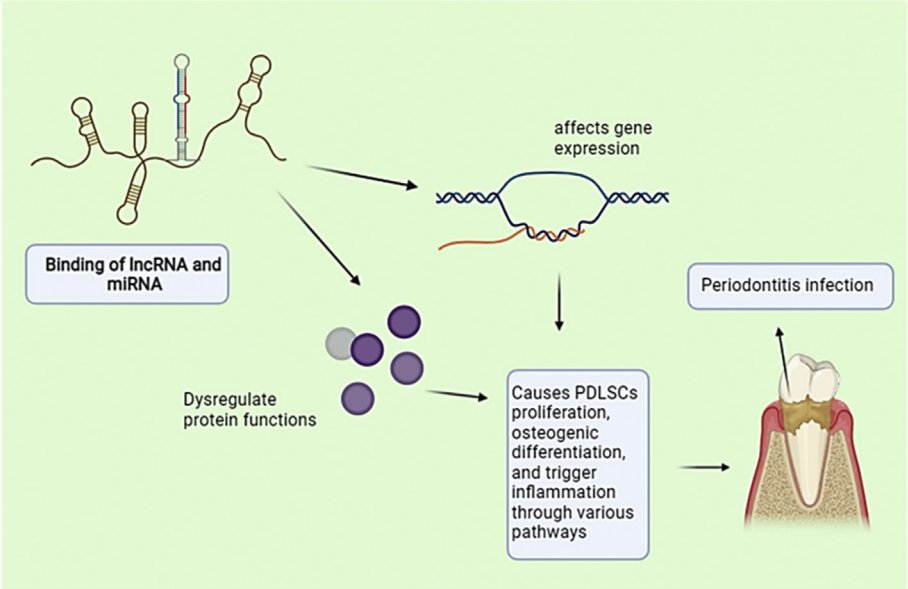

Figure 1 Schematic representation of the role of non-coding RNAs in periodontal pathogenesis. The binding of lncRNAs and miRNA causes differential expression of miRNA, which leads to dysregulated expression and inhibition of several proteins. Those proteins play a crucial role in osteogenic differentiation, PDLSC proliferation, and inflammation in periodontal infection.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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