INHIBITION OF PERIODONTAL DISEASES SPECIFIC MIRNAS: NEW THERAPEUTIC APPROACH

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Periodontal diseases comprise a wide range of inflammatory conditions affecting the supporting structures with a serious form called periodontitis (PD) that affects up to 50 % of people worldwide [1]. When left untreated, PD is one of the main causes of tooth loss. The first choice of rehabilitation for tooth loss is dental implants, but even up to 23 % of them do not adhere properly, and that results in peri-implantitis (PI), causing irreversible damage [2]. Multiple PD pathogenesis mechanisms are epigenetically regulated, and microRNAs (miRNAs) are considered as one of the key modulators that influences periodontal homeostasis [3]. This study aimed to identify PD-associated miRNAs in gingival tissue and evaluate the therapeutic potential of miRNA inhibition technology in managing PD and PI.

Microarray analysis of gingival tissue samples (N=16) revealed 140 upregulated miRNAs in inflamed gingival tissues compared to periodontally healthy tissues. Fifteen selected miRNAs were further analyzed by performing quantitative reverse transcription PCR in an extended cohort of gingival tissue samples (N=80). Analysis revealed that the levels of miR-146a-5p were significantly lower in PD-affected individuals compared to periodontally healthy participants. Severe forms of PD were associated with increased levels of miR-140-3p and -145-5p and decreased levels of miR-125a-3p. Moreover, the correlation between periodontal outcome parameters indicating the worse clinical status of PD and increased levels of miR-140-3p, -145-5p, and decreased levels of miR-125a-3p, was observed. MiRNAs abundantly expressed in gingival tissues, namely, miR-140-3p, -145-5p, -146a-5p, and -195-5p, were selected for further functional analysis.

Functional analysis of PD-specific miRNAs was performed in human bone marrow mesenchymal stem cells (hBM-MSCs). These cells were cultivated on cell culture plastic and medical titanium surface by transfection with inhibitors of selected miRNAs (antagomiRs). The efficacy of antagomiR treatment was evaluated under various transfection conditions by analyzing the expression levels of the targeted miRNAs. Analysis revealed that inhibitors of miR-140-3p significantly decrease the expression levels of miR-140-3p by 1.7-fold in cells cultured on plastic 2 days after transfection. While in cells cultured on medical titanium expression of miR-140-3p and -145-5p was most decreased 3 and 2 days after antagomiR transfection, respectively, although the expression differences were statistically non-significant ($P>0.050$).

The current study revealed that miRNAs play an important role in the pathogenesis of periodontal diseases. However, further studies are essential to evaluate the potential of miRNA inhibition technology in treating periodontal diseases.

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