

DOI: <https://doi.org/10.56936/18290825-2026.20v.2-50>**mRNA-BASED REGENERATION OF PERIODONTAL LIGAMENT FIBROBLASTS: A TRANSLATIONAL PILOT STUDY****JALALUDDIN M.¹, CALIAPEROMAL S.K.², JAYANTI I.³, PATIL M.³,
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ABSTRACT

Introduction: Periodontitis causes irreversible loss of supporting apparatus of the tooth, i.e., periodontal ligament. Although there has been promise in the growth factor therapies with recombinant proteins, including Fibroblast growth factor-2 (FGF-2) and the biological half-lives of these proteins, recombinant proteins have high costs, instability, and limited usability. Nucleoside-modified messenger RNA (mRNA) technology provides a new therapeutic modality approach with the use of host cell machinery to endogenously produce therapeutic proteins and, possibly, provide sustained bioactivity.

Material and Methods: Healthy premolars were used as sources of primary human periodontal ligament fibroblasts (n=10). The cells were separated into 3 conditions, which are Negative Control (untransfection), Positive Control (treated with recombinant human fibroblast growth factor-2 [rhFGF-2]) and Test Group (transfected with lipid nanoparticle-mRNA-FGF2). The proliferation of the cells was measured spectrometrically using Cell counting Kit-8 after 24, 48 and 72 hours. The migration capacity was measured based on a scratch wound healing assay. The expression of osteogenic and fibroblastic genes (COL1A1, POSTN, RUNX2) was determined by Reverse transcription quantitative polymerase chain reaction.

Results: mRNA-FGF2 showed a much higher proliferation at 72 hours than rhFGF-2 (Optical Density: 1.42 ± 0.11 vs. 1.15 ± 0.09 , $p < 0.01$), indicating longer protein synthesis. The highest percentage of wound close up at 24 hours was found in mRNA group ($88.4\% \pm 4.2$) when compared with the protein group ($76.1\% \pm 5.5$; $p < 0.05$). In addition, POSTN (Periostin) increased by 4.5-fold when mRNA was transfected compared to controls.

Conclusion: Intracellular exposure to lipid nanoparticle-encapsulated mRNA coding FGF-2 enhances better proliferation and migration in human periodontal ligament fibroblasts when compared to the exogenous application of proteins. In this pilot study, it is proposed that mRNA technology is a viable, powerful platform to next-generation periodontal regenerative therapies.

KEYWORDS: mRNA therapy; Periodontal regeneration; Fibroblast Growth Factor-2; Tissue engineering; Periodontal ligament fibroblasts

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