Pharmacodynamics of siRNARANKL and Oestrogen Loaded MSNs-CADY on Human Periodontal Ligament Stem Cells with Porphyromonas gingivalis infection

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Abstract
Background: Periodontitis irreversibly invades and destroys periodontal supporting tissues, loses the ability of periodontal regeneration and restoration, and eventually leads to tooth loosening and loss. Periodontal ligament stem cells (PDLSCs) hold great promises for periodontal tissue regeneration which was the potential target of periodontitis treatment, siRNARANKL and oestrogen can help PDLSCs maintain normal function, however, it was very difficult for siRNARANKL and oestrogen to get into PDLSCs. Here, Cell penetrating peptide CADY was modified on the surface of siRNARANKL and oestrogen loaded mesoporous silica nanoparticles (MSNs) to carry them into Porphyromonas gingivalis infected PDLSCs, Then further affect the proliferation of PDLSCs.

Methods: 120-150 nm Mesoporous silica nanoparticles (MSNs) was prepared, and the biocompatibility, loading capacity and drug release properity were tested; MSNs was modified by penetrating peptide CADY and the prepared MSNs/CADY was loaded with siRNARANKL and oestrogen; In vitro drug release of siRNARANKL/MSNs-CADY and oestrogen/MSNs-CADY was tested by using semi-permeable dialysis bag diffusion; Cellular uptake and internalization of FITC-Labeled MSNs and FITC-Labeled MSNs-CADY was observed by use of Laser confocal microscopy; Finally, the effect of siRNARANKL and oestrogen loaded MSNs-CADY on cell proliferation of Porphyromonas gingivalis infected human periodontal ligament stem cells was tested by MTT assay.

Results: according to the results, MSNs-CADY with a concentration of 6.25-200 ug/mL have no toxic to PDLSCs; 24.6 mg oestrogen and 0.5 mM siRNARANKL can be loaded into 1mg of MSNs-CADY; and drug loaded MSNs-CADY nanodrug carriers can release siRNARANKL and oestrogen stably for at least 48 h; After modification with cell penetrating peptide CADY, more MSNs-CADY can be taken by PDLSCs. siRNARANKL/oestrogen/MSNs-CADY can increase the proliferation of PDLSCs significantly.

Conclusion: siRNARANKL/oestrogen/MSNs-CADY constructed can significantly improve the cell proliferation of P-gingivalis infected PDLSCs, this nano drug carrier has the potential to be used in PDLSCs -based periodontitis treatment, this work provided a useful theoretical basis and therapeutic ideas for the treatment of periodontitis.

Full Text
Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the manuscript can be downloaded and accessed as a PDF.

Figures

|         | MSNs                  | MSNs-COOH               | MSNs-CADY               |
|---------|-----------------------|-------------------------|-------------------------|
| Zeta Potential | = 8.66               | = -38.24                | = 8.24                  |

Figure 1

Preparation and Characterization of MSNs, MSNs-COOH, MSNs-CADY.
Figure 2

Internalization characteristics of FITC-labeled MSNs and FITC-labeled MSNs@CADY. Blue fluorescence indicates nuclear staining with DAPI; green fluorescence indicates the localization of FITC-labeled MSNs, and red fluorescence indicates the staining of lysosomes by Lysotracker Red DND-99.
Figure 3

In Vitro Drug Releasing Property of siRNARANKL/MSNs-CADY and oestrogen/MSNs-CADY.

Figure 4

Cell Compatibility of MSNs-CADY.
Figure 5

The effect of MSNs/CADY/LRG on PDLSCs cell proliferation.