LOCALIZED OSTEOGENESIS VIA NANOPARTICLE-LOADED ELECTROSPUN PERIODONTAL MEMBRANE

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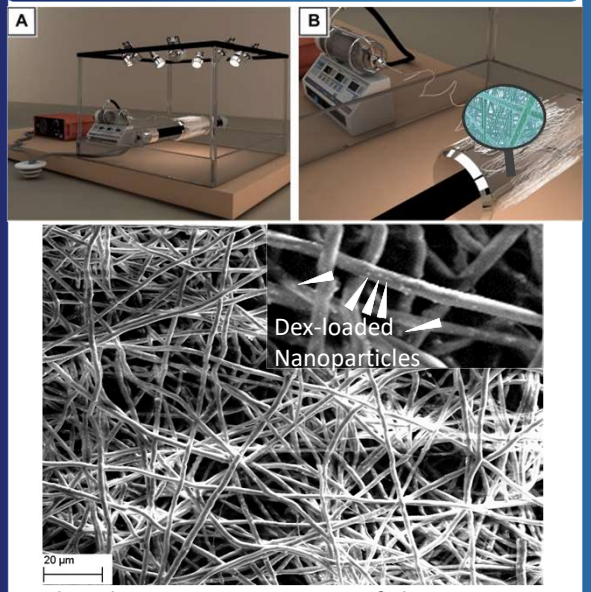
Introduction

Periodontitis is a prevalent chronic destructive inflammatory disease affecting tooth-supporting tissues in humans. Guided tissue regeneration (GTR), have been utilized to regenerate periodontium (e.g. periodontal ligament and alveolar bone) using a periodontal membrane. The periodontal membrane acts as a mechanical barrier that prevents/retards the apical migration of the gingival epithelium and allows periodontal ligament and bone tissues to selectively repopulate the root surface during healing. Current periodontal membranes lack osteo-conductivity and regenerative properties. Therefore, in the current study, we have designed a novel membrane-based drug delivery system for enhanced periodontal bone tissue regeneration.

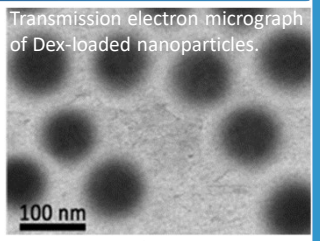
Materials & Methods

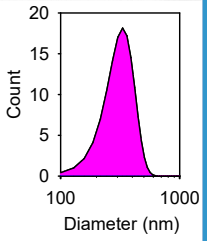


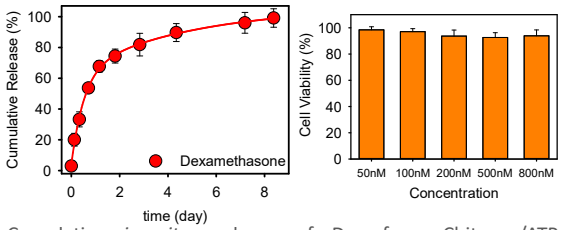
The schematic representation of electrospinning process to make nanofibrous matrices. Scanning electron microscopy of prepared fibers after conjugating with chitosan-based nanoparticles.

Results

Here, we have improved the conventional approach of localized delivery of osteoinductive and anti-inflammation agents to enhance the dental bone recovery while reducing the local inflammation. Chitosan-based polymeric nanoparticles, as one of the most promising choices for drug delivery systems, have been developed (diameter: 150 nm; Surface charge: +15 mV) which provide prolonged (4 weeks) release of small molecule drugs (here dexamethasone). These nanoparticles conjugated on the surface of biodegradable electrospun PLGA nanofiber membranes (fiber diameter: 400 nm, Mesh size: 5 um) to help implantation in the desired site of action (e.g., periodontal bone defects) while providing localized release.





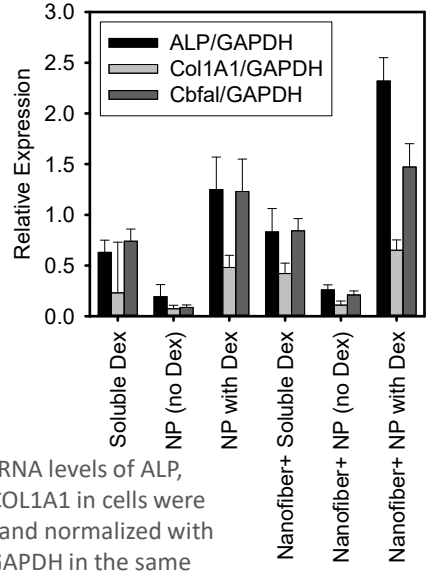


Cumulative *in vitro* release of Dex from Chitosan/ATP nanoparticles at 37 °C and pH of 7.4 (Mean ± SD, n > 3 independent experiments) (left). The effect of nanoparticle concentration without Dex on stem cell viability (based on MTT assay) (right) .

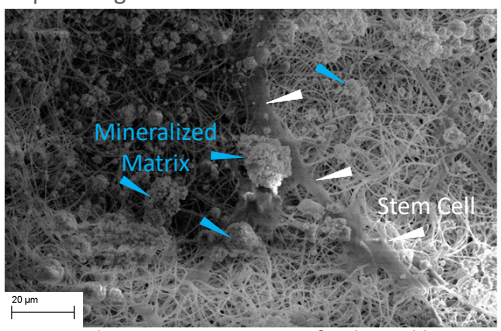
In vitro and *ex vivo* results confirm the functionality of the proposed approach to induce osteogenetic differentiation of human-derived mesenchymal stem cells after two and four weeks of culture in regular media as verified by microscopy (SEM), genetic (q-PCR) and chemical (Alizarin Red) methods. We believe that the insights learned from this work will lead to the discovery of new strategies to tune differentiation and localized treatment of periodontal bone defect.

Discussion

Effect of the nanoparticle delivery platform with or without presence of membrane on expression of osteogenic genes (ALP, cbfal, COL1A1 and GAPDH) after culturing of in human bone-marrow mesenchymal stem cells (hBMMSCs).



Relative mRNA levels of ALP, cbfal and COL1A1 in cells were compared and normalized with mRNA of GAPDH in the same sample using RT-PCR.



Scanning electron microscopy of cultured human bone-marrow mesenchymal stem cells (hBMMSCs) on nanofibrous matrix modified with Dexamethasone-loaded nanoparticles.