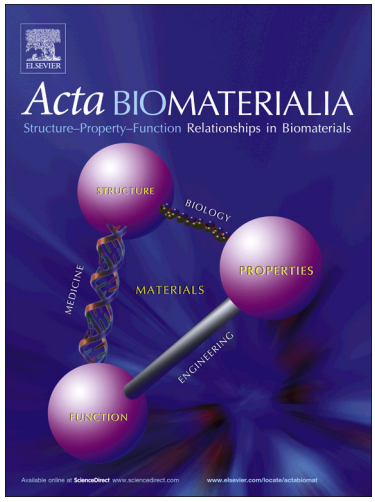

Full length article

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PII: S1742-7061(17)30803-6
DOI: https://doi.org/10.1016/j.actbio.2017.12.037
Reference: ACTBIO 5249

To appear in: *Acta Biomaterialia*

Received Date: 16 September 2017
Revised Date: 15 December 2017
Accepted Date: 22 December 2017

Please cite this article as: Soares, D.G., Zhang, Z., Mohamed, F., Eyster, T.W., de Souza Costa, C.A., Ma, P.X., Simvastatin and nanofibrous poly(l-lactic acid) scaffolds to promote the odontogenic potential of dental pulp cells in an inflammatory environment, *Acta Biomaterialia* (2017), doi: https://doi.org/10.1016/j.actbio.2017.12.037

Simvastatin and nanofibrous poly(L-lactic acid) scaffolds to promote the odontogenic potential of dental pulp cells in an inflammatory environment

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Abstract

In this study, we investigated the anti-inflammatory, odontogenic and pro-angiogenic effects of integrating simvastatin and nanofibrous poly(L-lactic acid) (NF-PLLA) scaffolds on dental pulp cells (DPCs). Highly porous NF-PLLA scaffolds that mimic the nanofibrous architecture of extracellular matrix were first fabricated, then seeded with human DPCs and cultured with 0.1 μM simvastatin and/or 10 μg/mL pro-inflammatory stimulator lipopolysaccharide (LPS). The gene expression of pro-inflammatory mediators (TNF-α, IL-1β and MMP-9 mRNA) and odontoblastic markers (ALP activity, calcium content, DSPP, DMP-1 and BMP-2 mRNA) was quantified after long-term culture *in vitro*. In addition, we evaluated the scaffold's pro-angiogenic potential after 24 hours of *in vitro* co-culture with endothelial cells. Finally, we assessed the combined effects of simvastatin and NF-PLLA scaffolds *in vivo* using a subcutaneous implantation mouse model. The *in vitro* studies demonstrated that, compared with the DPC/NF-PLLA scaffold constructs cultured only with pro-inflammatory stimulator LPS, adding simvastatin significantly repress the expression of pro-inflammatory mediators. Treating LPS+ DPC/NF-PLLA constructs with simvastatin also reverted the negative effects of LPS on expression of odontoblastic markers *in vitro* and *in vivo*. Western blot analysis demonstrated that these effects were related to a reduction in NFkBp65 phosphorylation and up-regulation of PPARγ expression, as well as to increased phosphorylation of pERK1/2 and pSmad1, mediated by simvastatin on LPS-stimulated DPCs. The DPC/NF-PLLA constructs treated with LPS/simvastatin also led to an increase in vessel-like structures, correlated with increased VEGF expression in both DPSCs and endothelial cells. Therefore, the combination of low dosage simvastatin and NF-PLLA scaffolds appears to be a promising strategy for dentin regeneration with inflamed dental pulp tissue, by minimizing the inflammatory reaction and increasing the regenerative potential of resident stem cells.

The regeneration potential of stem cells is dependent on their microenvironment. In this study, we investigated the effect of the