

Application of stem cells derived from the periodontal ligament or gingival tissue sources for tendon tissue regeneration

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Statement of Purpose: Tendon injuries are often associated with significant dysfunction and disability due to tendinous tissue's very limited self-repair capacity and propensity for scar formation. Dental-derived mesenchymal stem cells (MSCs) in combination with appropriate scaffold material present an alternative therapeutic option for tendon repair/regeneration that may be advantageous compared to other current treatment modalities. The MSC delivery vehicle is the principal determinant for successful implementation of MSC-mediated regenerative therapies.

Methods: In the current study, a co-delivery system based on TGF- β 3-loaded RGD-coupled alginate microspheres was developed for encapsulating periodontal ligament stem cells (PDLSCs) or gingival mesenchymal stem cells (GMSCs). The capacity of encapsulated dental MSCs to differentiate into tendon tissue was investigated *in vitro* and *in vivo*. Encapsulated dental-derived MSCs were transplanted subcutaneously into immunocompromised mice.

Results: Our results revealed that after 4 weeks of differentiation *in vitro*, PDLSCs and GMSCs as well as the positive control human bone marrow mesenchymal stem cells (hBMMSCs) exhibited high levels of mRNA expression for gene markers related to tendon regeneration (Scx, DCn, Tnmd, and Bgy) via qPCR measurement. In a corresponding *in vivo* animal model, ectopic neo-tendon regeneration was observed in subcutaneous transplanted MSC-alginate constructs, as confirmed by histological and immunohistochemical staining for protein markers specific for tendons. Interestingly, in our quantitative PCR and *in vivo* histomorphometric analyses, PDLSCs showed significantly greater capacity for tendon regeneration than GMSCs or hBMMSCs ($P < 0.05$).

Conclusions: Altogether, these findings indicate that periodontal ligament and gingival tissues can be considered as suitable stem cell sources for tendon engineering. PDLSCs and GMSCs encapsulated in TGF- β 3-loaded RGD-modified alginate microspheres are promising candidates for tendon regeneration.

numbers in parentheses. For example: (Dodd LG. Am J Clin Pathol. 1990;93:141-144.)