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Title: Design and fabrication of injectable alginate hydrogel microstrands for mesenchymal stem cell delivery in salivary gland tissue regeneration

Abstract: Fibrosis is a pathological wound healing process, driven by excessive accumulation of extracellular matrix following tissue remodeling. Fibrosis occurs in diseased or damaged salivary glands caused by several conditions, such as Sjogren's syndrome or radiation for head and neck cancers. Having a better insight on the cellular and molecular progression of the fibrosis will allow to model new therapeutic approaches as it prevents salivary gland tissue regeneration and function. Pharmacological, tissue engineering and cell-based regeneration strategies have been widely explored as a way to restore lost salivary gland function. Among the cell-based therapies, exploitation of mesenchymal stem cells (MSC) for salivary gland regeneration has been actively pursued due to its anti-fibrotic and anti-inflammatory properties. However, the therapeutic potential of MSC-based therapies relies on successful migration and engraftment of cells to the diseased or injured site of the tissue or organ. Despite its immunomodulatory properties, MSCs need a delivery vehicle, which can support their growth and allow to maintain their functional characteristics (phenotype) during transplantation. FDA-approved, biocompatible alginate hydrogels in the form of microstrands have great potential to deliver MSCs at the site of injured tissue due to its extracellular mimicking properties and ease of chemical modulations. Microstrands of diameters ≤200 micrometers do not limit diffusion of oxygen, cytokines, and growth factors unlike bulk hydrogels. Preliminary studies showed that 1) alginate hydrogel microstrands can be fabricated reproducibly using syringe-in-syringe and syringe-in-container devices; and 2) alginate hydrogel microstrands support high-density cell growth of MSC-like cells with high cell viability, indicate the feasibility of producing injectable alginate hydrogel microstrands for salivary gland regeneration.