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Comment

Regenerative Endodontics and the promise beyond dental pulp disease repair.

Ziyad S. Haidar.[1,2]

Affiliations: [1]BioMAT'X, Facultad de Odontología, Universidad de los Andes, Santiago, Chile. [2]CIIB, Facultad de Medicina, Universidad de los Andes, Santiago, Chile.

Corresponding author: Ziyad S. Haidar. Facultad de Odontología, Universidad de los Andes, Mons. Álvaro del Portillo 12.455. Las Condes, Santiago, Chile. Phone: (56-2)26181372. Ext: (56-2) 22149468. E-mail: zhaidar@uandes.cl

The dental pulp is a multi-structural soft tissue composed of fibroblasts, odontoblasts, lymphocytes, endothelial cells, amongst others; with prominent formative, sensorial, and protective functions. Pulpitis is a painful inflammatory (necrotic) disease caused by untreated dental decay/caries, trauma and multiple restorations; often irreversible/unrecoverable, due to insufficient vascularization, mainly because of the anatomy of the pulp chamber: a small root canal in volume and a narrow apical foramen.[1]

Recently, endodontic regenerative approaches, strategies and biomaterials for treating dental pulp diseases have been receiving ample attention.[3] While regenerative medicine concepts are clear (*i.e.* stem cells/growth factors/scaffold complex transplantation into the pulp chamber), the main obstacle seems to be associated with identifying the "ideal" scaffold suitable for biologically-functional pulp tissue regeneration; providing a 3-D spatio-temporal structure and a *mimicked* extracellular matrix (ECM) environment (space:time) for the stem cells to survive, migrate, proliferate and differentiate, within the prepared pulp canal.[1,2]

Indeed, we witness the design, development and utilization of various scaffolds/bio-scaffolds for dental pulp regeneration, primarily based on prominent natural/synthetic polymers and co-polymers (biocompatible/biodegradable) including collagen and poly(lactic acid).[1,2] Yet, the literature concludes extant limitation in ability to form dentin, mainly ascribed to lack of dental pulp ECM. Hence, there is a need to construct a regenerative scaffolding matrix containing dental pulp ECM, basically to: (1) selectively bind/localize cells; (2) contain dose-responsive vital cytokines with release-controlled pharmacokinetics; (3) promote odontoblast differentiation; (4) control/regulate dental pulp stem/progenitor cell fate and metabolism; and (5) facilitate correct/functional spatio-temopral dentin formation (undergo safe and timely biodegradation). Consequently, consider scaffold porosity and pore-size (high, *preferred*) facilitating cell seeding/diffusion and effective transport of nutrients, oxygen, and waste; whilst maintaining an adequate physico-mechanical strength.[2-4] So, it is critical to master thorough biomaterial and pharmaceutic knowledge.

Soon, owing to advancements in *biomimetic* scaffold fabrication technology; whether via combining materials or through utilizing CAD/3-D printing, clinicians shall witness inductive matrices with well-controlled complex behavior; a promising future in completely-functional regenerative endodontics. Keep an eye on acellular (de-cellularized) natural ECM scaffolds combined with human-derived dental pulp stem cells for bio-active pulp tissue regeneration.

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