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Revascularization promoted by platelet pro-angiogenic factors or hyaluronan oligomers – A step towards endodontic regeneration using injectable systems

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INTRODUCTION: Revascularization of pulp canal after endodontic treatment attains to rescue teeth from mid-term extraction fate, and can be promoted by the injection of hydrogels containing adequate cues. Herein are explored the proangiogenic effect of platelet-origin mediators modulated release [1] or hyaluronan oligomers instructive cues [2] within hydrogels aiming endodontic regeneration.

METHODS: Hyaluronic acid (HA) hydrogels incorporating PL were produced by mixing 2% aldehyde-modified HA solution containing aldehyde-functionalized cellulose nanocrystals (CNCs) with 2% hydrazide-functionalized HA dissolved in human platelet lysate (PL). Were assessed the sprouting of human dental pulp cells (hDPCs) or DPCs/HUVECs 1:1 pellets encapsulated in the HA hydrogels, and the neovascularization in a chicken choriollantoic membrane (CAM) assay. Also, low (LMW) or high (HMW) molecular weight (6 kDa and 230 kDa; Lifecore) HA were immobilized over methacrylated gelatin hydrogels (GelMA) and the response of HUVECs in terms of viability and arrangement analyzed.

RESULTS & DISCUSSION: PL incorporation enhanced the sprouting of DPCs both in single and co-cultures ($p > 0.001$). Moreover, the combined effect of PL and DPCs encapsulation promoted the ingrowth of vascularized tissue into the hydrogels. The immobilization of LMW-HA over GelMA hydrogels enhanced the metabolic activity and promoted the organization of HUVECs into capillar-like structures.

CONCLUSIONS: Our findings from in vitro studies show that both the incorporation of human-origin proangiogenic growth factors and the creation of instructive paths of HA oligomers within injectable hydrogels, might promote the revascularization required for endodontic regeneration.

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