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Development of Hyaluronic Acid/Collagen-Based Hydrogel for Intervertebral Disc Regeneration: An Implication for the Treatment of Low Back Pain

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INTRODUCTION:

The imbalance of extracellular matrix (ECM) homeostasis is a hallmark of disc degeneration, which can alter hydration and cellularity, and increase inflammation, thus contributing to discogenic pain[1]. The ECM-based biomaterials provide a better platform to mimic the 3D disc microenvironment in supporting the transplantation of stem cells to promote tissue regeneration and target pain. Nevertheless, limited information detailing *in vitro* pre-conditioning human umbilical cord-derived Wharton Jelly mesenchymal stem cells (MSCs) in 3D HA/COLII hydrogel towards nucleus pulposus (NP) phenotype and modulate pain.

MATERIALS & METHODS:

We developed a tuneable 3D hyaluronic acid (HA)/type II collagen (COLII) hydrogel by varying macromolecule weight ratios of HA: COLII, 1:9 and 4.5:9. We characterised hydrogel for degradation, stability and swelling properties. We determined the cell morphology and viability as well as NP phenotypic markers on MSC-encapsulated hydrogel. Post-implantation of hydrogel in a surgically induced disc injury model of pain in the rat tail, we assessed the body weight for general health status and nociceptive behaviour for mechanical allodynia using the von Frey test in rats over 28 days.

RESULTS:

We observed that all hydrogel formulations were hydrolytically stable with similar enzymatic degradation profiles over time. The swelling property of the 4.5:9 HA/COLII hydrogel was significantly greater than that of the 1:9 HA/COLII hydrogel. We found higher cell viability of MSCs up to 14 days in culture. We informed the differentiation of MSCs toward NP-like cells, indicated by the round morphology shape of the cells within the 3D hydrogel system with up-regulation of SOX9 marker for NP phenotype **(Figure 1)**. *In vivo*, we found that disc injury-induced mechanical allodynia in rats, whereas hydrogel treatment suppressed this response.

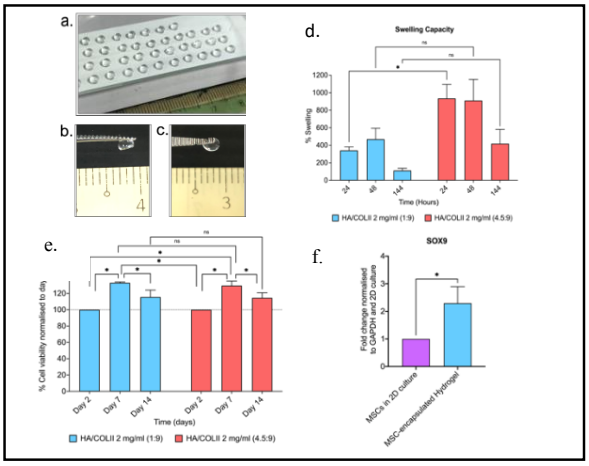

Figure 1: The development of HA/COLII hydrogel. (a) Photograph of the hydrogel with weight ratios of HA: COLII at 1:9 (b) and 4.5:9 (c). (d) Swelling property of the hydrogel. (e) Cell viability over 14 days in culture. (f) Up-regulation of SOX9 expression. $p<0.05$, two-way ANOVA and t-test, $n=3$.

DISCUSSIONS:

The 3D microenvironment of hydrogels becomes favourable for the cells to survive and support MSC differentiation towards NP phenotype.

CONCLUSION:

We successfully develop a tunable hydrogel that mimics the NP microenvironment in facilitating the differentiation of MSCs toward NP-like cells. Our findings indicate that hydrogel could support MSC transplantation to promote disc regeneration and target pain.

REFERENCES:

1. Mohd Isa, I. L. *et al.*. *Adv. Healthc. Mater.* **11**, e2102530 (2022).