

COLLEGE OF DENTAL MEDICINE



Heparin-conjugated Bio-glue to Promote Healing of Lubricin-Coated Fibrocartilage Injuries

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INTRODUCTION

- Functional regeneration of fibrocartilaginous tissues, including knee meniscus and TMJ disc, is an acute clinical burden.
- Tears in avascular region of meniscus and perforation in TMJ discs have poor healing capabilities, frequently leading to detrimental joint damages.
 We have recently developed a regenerative strategy for meniscus and TMJ disc by recruitment of endogenous stem/progenitor cells via a connective

RESULTS

Lap shear properties significantly increased with Conjugated Hep-Fib-Gen even with lubricin coating



tissue growth factor (CTGF)-loaded bio-glue mixed with PLGA microspheres (μ S)-encapsulating transforming growth factor beta 3 (TGF β 3) (**Fig. 1**).

TGFβ3 in PLGA μS





Fibrocartilaginous tissue integration

Mesenchymal Stem/Progenitor Cells

Figure 1. *In situ* regeneration of fibrocartilaginous tissues such as knee meniscus and TMJ disc by stem cell recruitment.

- Clinically, however, exposure to lubricin in synovial fluids has harmful effects on the healing of fibrocartilaginous tissues, supported by our previous works.
- This study is designed to advance our approach to fibrocartilage regeneration by tethering lubricin on torn tissue surfaces.
- Given that the heparin binding domain at N terminal of lubricin, we applied a heparin-conjugated fibrin gel cross-linked with genipin to our established explant model of avascular meniscus tear healing

Figure 3. Lap Shear Tests of different bio-glues with lubricin-coated meniscus strips (**A**). Lap shear modulus (**B**) (n=8-15 per group: p<0.0001 compared to all groups). %Change in shear strength by lubricin coating compared to (PBS control) no coating samples (**C**) (n=8-15 per group; p<0.001 compared to no-coating control.

Conjugated Hep-Fib-Gen improves healing of meniscus pre-coated with lubricin



METHODS

Strategies to enable healing of lubricin-infiltrated meniscus



Figure 4. Healing of avascular meniscus tears by MSC recruitment with CTGF and TGF β 3 (μ S) administered in various bio-glues for 4 wks: Histology with Picrosirius Red (PR) (**A**), and tensile modulus (**B**) (n=5 per group: *:p<0.01 compared to all groups), % changes in tensile modulus (**C**) and strength (**D**) by lubricin pre-coating (n=5 per group; *:p<0.01 compared to no-coating (PBS control).

DISCUSSION AND CONCLUSIONS

Figure 2. Strategy to improve healing of lubricin infiltrated meniscus by heparin conjugated fibrin cross-linked with genipin.

- Our findings suggest that heparin conjugation further increased the mechanical properties of fibrin cross-linked with genipin when applied to lubricin infiltrated fibrocartilage.
- One of the limitations of this study was that there was a relatively large variance in the initial mechanical properties of conjugated Hep-Fib-Gen as compared to the other bio-glues, which may require further refinement of purity in the carbodiimide synthesis process.
 In conclusion, Conjugated Fib-Gen may serve as an efficient bio-glue to promote MSC healing of clinically relevant injuries on fibrocartilaginous tissues including TMJ disc and knee meniscus.

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