OFFICIAL ABSTRACT and CERTIFICATION

Heparin-Conjugated Bioactive Glue for Regeneration of Lubricin-infiltrated Meniscus Tears by Recruitment of Stem/Progenitor Cells

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Meniscus injuries occur in over one million Americans each year and are one of the most important contributing factors to knee osteoarthritis (OA). The presence of lubricin is in meniscal injuries is detrimental to the avascular healing of meniscus due to the lubricating properties that negate regeneration. By utilizing the heparin binding domain at the N-terminal of lubricin, we attempted to circumvent the affects of lubricin through the use of heparin-conjugated fibrin gel cross-linked with genipin to establish a successful avascular tissue healing effect. Menisci from mature bovine knee joints were treated with varying mixtures of gels and used for lap shear tests. Separate tissue was incised, loaded with gels, and cultured. After 4 weeks, samples were harvested and underwent histology, biochemical assays, and multi-scale mechanical tests. Compared to the other material combination gels, conjugated Hep-Fib-Gen consistently outperformed the other groups. Reduction in shear strength by 14%-33% was observed in other groups with lubricin coated tissues, while conjugated Hep-Fib-Gen display ~68% increase in shear modulus. Additionally, when lubricin coated, conjugated Hep-Gen-Fib displayed superior tissue integration. This study suggested that heparin conjugation into Fib-Gen hydrogel strengthened initial bonds in lubricin coated meniscus tears, leading to improved avascular healing, and mechanical properties. In conclusion, conjugated Hep-Fib-Gen may serve as efficient bio-glue to support healing of clinically relevant meniscus tears by endogenous stem cell recruitment.

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