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HAPLN1 Exhibits Chondroregenerative Ability in Injury-induced Osteoarthritic Animals Through ALK5-SMAD2/3 Signaling in Articular Chondrocytes

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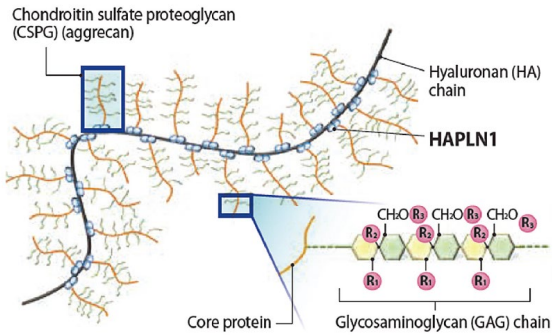
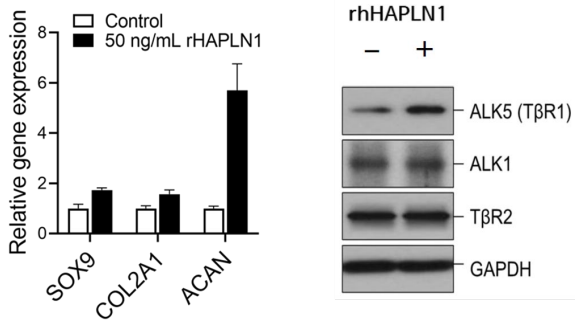
I. Background

Hyaluronan and proteoglycan link protein 1 (HAPLN1) has been known to play a role in the extracellular matrix (ECM) integrity by stabilizing the physicochemical interaction between aggrecan and hyaluronic acid chain.



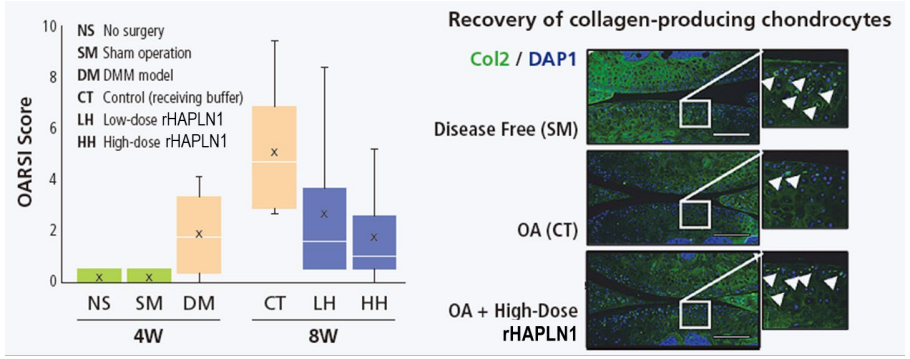
II. *in vitro* studies

Human primary chondrocytes treated with rHAPLN1 showed significantly increased mRNA levels of SOX9, type II collagen, and aggrecan. Mouse primary chondrocytes treated with rHAPLN1 showed a significant increase in the protein level of ALK5, but the level of the ALK1 was not changed.



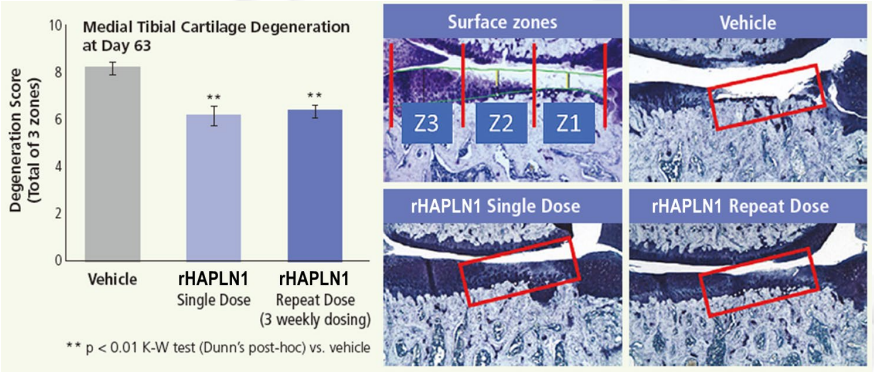
III. *in vivo* efficacy study in mouse OA (DMM)

rHAPLN1 treatment showed an improvement in OARSI score in a dose-dependent manner. Immunofluorescence analysis revealed an increased population of articular chondrocytes producing type II collagen in the rHAPLN1-treated group.



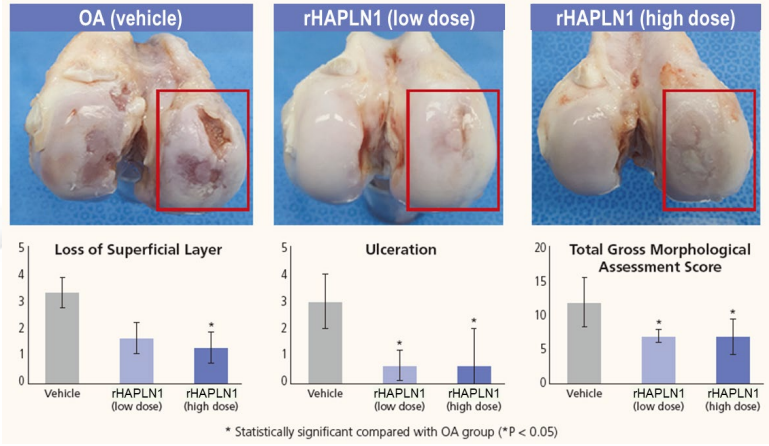
IV. *in vivo* efficacy study in rat OA (Complete MMT)

rHAPLN1 alleviated cartilage degeneration as measured by depth ratio in middle zone of tibial plateau.



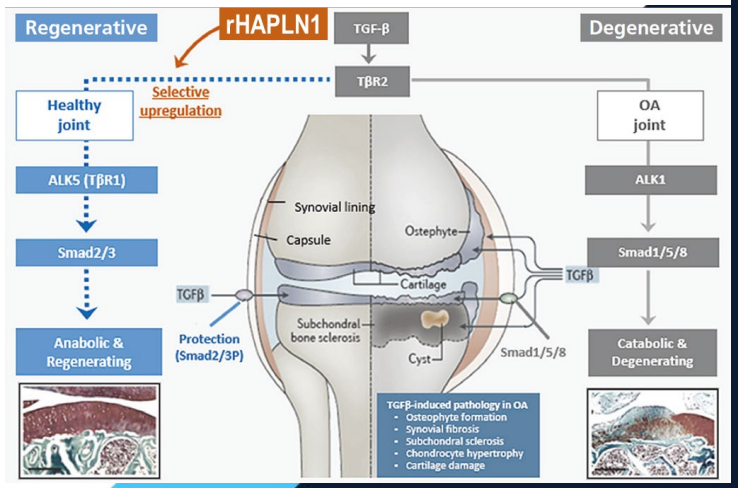
V. *in vivo* efficacy study in goat OA (ACLT+MMx)

Both the low- and high-dose of rHAPLN1 revealed a clear improvement in the gross morphological assessment of the femoral condyle. rHAPLN1 also showed a preventive effect against the loss of the superficial layer and the development of ulceration.



VI. Conclusion

It is well known that the ALK5-SMAD2/3 signaling pathway is a key mechanism in cartilage regeneration and homeostasis. This encouraging evidence suggests that HAPLN1 is able to reinforce the matrix integrity as well as the mechanical structures, and further cell-matrix interactions that give rise to intracellular signaling.



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