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

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.

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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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