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Identification of Lysyl Oxidase on Repression of Inflammation for Promoting Anterior Cruciate Ligament Remodeling

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Abstract: At present, anterior cruciate ligament (ACL) damage repair is still a huge challenge. Our previous studies indicated that the Lysyl oxidase (LOX) were significantly reduced in injurious ACL fibroblasts, which is the major reason for its poor healing ability. The main purpose of our study was to detected the potential of LOX to act as an anabolic agent in injured ACL. The effect of LOX on the ACL at a concentration of 20ng/mL was investigated. The molecular mechanisms and signaling pathway were elucidated by RNA-sequencing, q-PCR and western blotting. For the *in vivo* study, the LOX was injected into the joint cavity after injury, and the were perfoemed on the histological analysis. Results shown that the LOX promotes the proliferation of ACL fibroblasts and inhibits the apoptosis of cells by inflammation. In addition, exogenous LOX can significantly reduce the expression of inflammatory factors such as IL-1β, IL-6 and matrix metalloproteinases (MMPs).RNA-sequencing revealed 168 differentially expressed genes (DEGs) with 23 that were up-regulated and 146 that were down-regulated in the control vsTNF-α; 228 differentially expressed genes (DEGs) with 192 that were up-regulated and 36 that were down-regulated in the TNF-α vs TNF-α+LOX. LOX also inhibited TNF-α-induced MTPN expression. The siRNA silencing revealed that MTPN was the target of LOX in terms of its anti-inflammatory effect via non-classical NF-κB pathway.LOX treatment of injured ACL tissue in rabbits 4 weeks after surgery, H&E staining histological analysis showed that LOX treatment had a significant effect on ACL tissue reconstruction. Four weeks after injection of LOX, the appearance and physiological structure of the ACL tissue was more integrated compared to that of the control. The maximum fracture force of the ACL was significantly higher than that of the control group. LOX treatment promotes the repair of damaged ACL by regulating cell proliferation, extracellular matrix synthesis, and inhibition of inflammatory responses.

Keywords: ACL; damage repair; LOX; anti-inflammatory; RNA-sequencing

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