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The effect of integrin $\alpha 1\beta 1$ on Smad2/3 and phosphoSmad2/3 expression in murine chondrocytes

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Abstract

Background: Chondrocytes, the cells of cartilage, maintain and repair the extracellular matrix by secreting and degrading proteins such as collagen type II and aggrecan.[1] Integrins are transmembrane adhesion proteins that cells use to both bind to and sense the extracellular matrix. Chondrocytes express many different types of integrin molecules and this study focuses on the collagen II and VI receptor integrin $\alpha 1\beta 1$. Transforming growth factor-beta (TGF-β) stimulates chondrocytes to repair cartilage through a number of intracellular pathways of which the Smad2/3 pathway is a known major fibrotic pathway.[2] An excess build-up of bony tissue leads to the formation of fibrotic osteoarthritis (OA) in integrin $\alpha 1$-null mice at an earlier age and to a more severe extent than wild type controls.[3] Based on these data we hypothesize that integrin $\alpha 1\beta 1$ controls the sensitivity of chondrocytes to TGF-β. When integrin $\alpha 1\beta 1$ is missing chondrocytes are oversensitive to TGF-β, possibly through Smad2/3 pathway up regulation. The objective of this experiment is to measure the protein levels of Smad2/3 and phosphoSmad2/3 in wild type and integrin $\alpha 1$-null murine chondrocytes. We expect up regulation of phosphoSmad2/3 in integrin $\alpha 1$-null mice compared to wild-type controls.[3]

Methods: Enzymatically isolated chondrocytes from 4-6 month old mice were sonicated and the released protein concentrated through centrifugal filtration. Protein was measured through Western-blotting analysis.

Results: Integrin $\alpha 1$-null murine chondrocytes contain Smad2.

Discussion: Smad2 has been shown in wild-type chondrocytes, but not previously in integrin $\alpha 1$-null chondrocytes.[4] However, Smad2/3 and up-regulated phosphoSmad2/3 have been found in integrin $\alpha 1$-null renal medulla cells.[2] With further development of techniques, Smad3 and phosphoSmad2/3 will be measured in wild-type and integrin $\alpha 1$-null murine chondrocytes and thus the pathway for fibrotic OA in integrin $\alpha 1$-null mice can be further determined.

References

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