통증 및 근골격재활

게시일시 및 장소 : 10 월 18 일(금) 08:30-12:20 Room G(3F)

질의응답 일시 및 장소 : 10 월 18 일(금) 10:00-10:45 Room G(3F)

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Pain Mediators Can Affect Regeneration Potency of Tendon Derived Stem Cell in Tendinopathy

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Introduction

Histologically, tendinopathic tissue shows a failed healing status characterized by tissue metaplasia including chondrocyte phenotypes, fatty infiltration, and bony deposits. Tendon-derived stem cells (TDSCs) in tendons are responsible for tenogenesis and tendon healing. Nontenogenic differentiation of TDSCs have been suggested as pathogenesis of tendinopathy. Therefore, regulatory factors for either tenogenic or nontenogenic differentiation of TDSC could be targets for the treatment of tendinopathy. Pain mediators, such as substance P and macrophage migration inhibitory factor (MIF), have been increasingly discussed as an important factor in the pathogenesis of tendinopathy. The purpose of this study was to evaluate whether the pain mediator associated with pain signal pathway affects tenogenic differentiation of TDSC.

Methods and Materials

For in vivo study, we established tendinopathy rat model with supraspinatus overloading exercise. The supraspinatus tendon tissues were harvested and prepared for real-time reverse transcription polymerase chain reaction (RT-PCR). For the isolation of TDSC, we stripped off the tendon sheath of SD rats and cut tendon tissues into small pieces and digested with collagenase and single-cell suspensions were cultured in DMEM, supplemented with FBS and antibiotics. For in vitro study, Isolated TDSC were treated with recombinant Substance P and recombinant MIF, and small interference RNA (siRNA) transfected MIF for knockdown of MIF, and prepared for real-time RT-PCR.

Results

For in vivo study, as compared to sham rats, tenogenesis related genes, such as SCX, Egr1, Tnmd (tenomodulin) and collagen type 1, and pain mediators in pain signal pathway, such as MIF and TRPV1, and proinflammatory cytokine, TNF-a was up-regulated in tendinopathy rats. On the other hand, there was no differences of chondrogenesis related genes, such as BMP2, aggrecan and Sox9, between the two groups. (Fig.1) For in vitro study, compared with control TDSC, Substance-P treated TDSC culture mediums showed down-regulated expression of tenogenic genes (SCX, Egr1, Tnmd and collagen

type 1), and up-regulated expression of pain mediators (MIF and CGRP). In terms of chondrogenic genes, the expression of BMP2 and aggrecan was similar between Substance P treated TDSC media and control except Sox9 (up-regulated in Substance-P treated TDSC). In addition, recombinant MIF treated TDSC culture mediums showed increased CGRP and chondrogenic genes expression (BMP2, aggrecan and Sox9) whereas tenogenic genes (SCX, Egr1, Tnmd and collagen type 1) were decreased, compared with control TDSC. Intriguingly, siRNA-transfected knockdown of MIF in TDSC showed findings in reverse as with recombinant MIF. (Fig. 2)

Conclusion

Our results suggest that pain mediator (Substance-P and MIF) is associated with pathogenesis of tendinopathy via suppression of tenogenic differentiation of TDSC, rather than aberrant nontenogenic differentiation of TDSC.

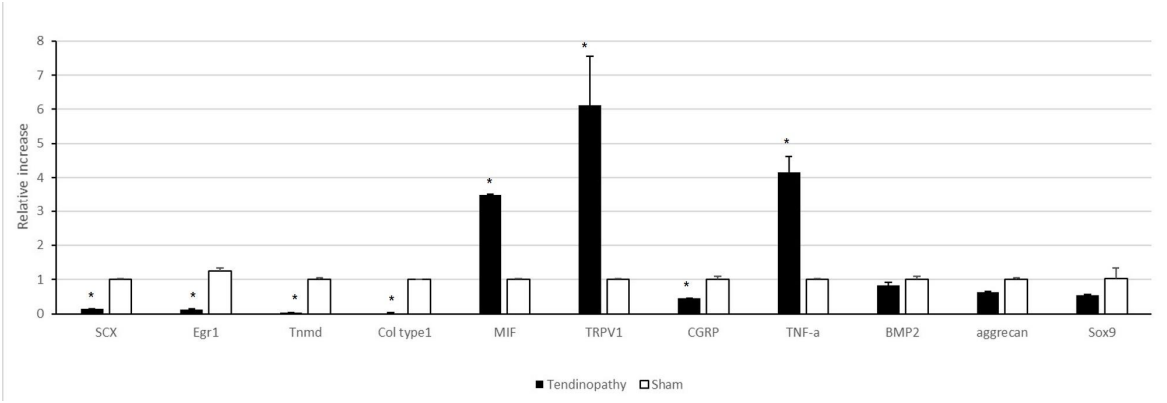

Fig.1

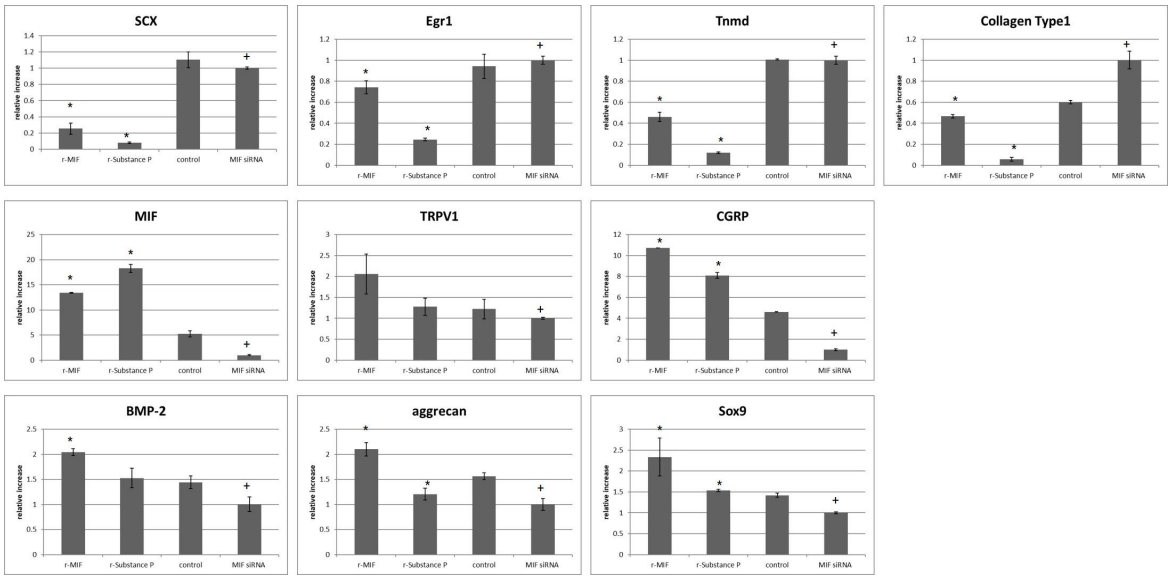

Fig.2