



Title	Degenerated meniscus alters knee osteoarthritis-related gene expression in articular chondrocytes through paracrine mechanisms
Author(s)	郭, 博
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論文内容の要旨

Synopsis of Thesis

氏 名 Name	郭 博
論文題名 Title	Degenerated meniscus alters knee osteoarthritis-related gene expression in articular chondrocytes through paracrine mechanisms (変性膝半月板は、パラクリン機構を介して関節軟骨細胞における変形性膝関節症関連因子の遺伝子発現を変化させる)
論文内容の要旨	
〔目 的(Objective)〕 The biomechanical properties of the meniscus are involved in the pathogenesis of knee osteoarthritis (KOA), however, the biological role of a degenerated meniscus in KOA is unclear. This study examined the effects of degenerated meniscus on articular chondrocytes.	
〔方法ならびに成績(Methods/Results)〕 Methods: Human menisci and articular chondrocytes were obtained from 13 patients with KOA who underwent total knee arthroplasty (TKA). Human meniscus pieces were cultured as explants, and articular chondrocytes were isolated by enzymatic digestion and cultured. For the experiments, part of meniscal tissues were stimulated with IL-1 β . A co-culture model was set up using transwells to allow for a paracrine effect without direct cell contact. Moreover, culture supernatant from IL-1 β -stimulated menisci was collected and used to culture chondrocytes at different concentrations. Total RNA was extracted from the chondrocytes for RNA sequencing and quantitative real-time PCR (qPCR) to analyze gene expression. Immunofluorescence staining was also performed to visualize protein expression of MMP3 and COX2. The data were statistically analyzed using independent sample t-tests, with significance set at $p < 0.05$. Results: RNA sequencing and RT-qPCR analyses showed that co-culturing chondrocytes with degenerated menisci led to increased expression of inflammatory factors, such as IL-6, IL-7R, CCL-2, and CXCL-6, and matrix metalloproteinases (MMP-3 and MMP-13). In contrast, the expression of aggrecan (ACAN), a key cartilage component, was reduced. These gene expression changes were more pronounced if co-cultured with IL-1 β -stimulated degenerated meniscus. Furthermore, culture supernatant from IL-1 β -induced inflammatory human degenerated meniscus caused similar gene expression changes in articular chondrocytes as the co-culture. Immunofluorescence staining of the cells confirmed a positive correlation between the percentage of degenerated meniscal culture supernatant in the culture medium and MMP3- and COX2-positive articular chondrocytes.	
〔総 括(Conclusion)〕 These findings suggest that degenerated human meniscal tissue induces inflammatory and degenerative changes in articular chondrocytes through a paracrine mechanism, potentially contributing to KOA pathogenesis.	

論文審査の結果の要旨及び担当者

(申請者氏名) 郭 博				
論文審査担当者	(職)		氏 名	
	主 査	大阪大学教授	中 田 研	署名
	副 査	大阪大学教授	柳 澤 琢 史	署名
	副 査	大阪大学教授	島 田 昌 一	署名
論文審査の結果の要旨				
本研究は、変形性膝関節症（KOA）の病態における変性膝半月板の関与について、KOA患者から得られた組織と細胞を用いて検討した。主な結果として、ヒト変性半月板と共培養した関節軟骨細胞では、炎症関連因子や軟骨基質分解酵素（マトリックスメタロプロテアーゼ）などのKOA関連因子の遺伝子発現が促進された。また、半月板培養上清を含んだ培地にて培養した関節軟骨細胞でも類似の遺伝子発現パターンが観察され、これらのタンパク質の発現が誘導された。以上の結果により、変性半月板組織がパラクリン機構を介して関節軟骨細胞の遺伝子発現を変化させ、KOA発症に関与する可能性が示された。本研究で得られた結果は、KOA病態をより深く理解するために重要であり、将来的にKOAに対する新規治療法の開発の礎になりうる。ゆえに、博士（医学）の学位授与に値する。				