Long Noncoding RNA Related To Cartilage Injury Promotes Chondrocyte Extracellular Matrix Degradation In Osteoarthritis

Liu Q¹, Ao YF¹

¹ Peking University Third Hospital Institute of Sports Medicine
liuqiang_lq1987@163.com

Introduction:
Long noncoding RNAs (lncRNAs) play crucial regulatory roles in diverse biologic processes, but knowledge of lncRNAs in osteoarthritis (OA) is limited. The aim of this study was to identify lncRNA expression in articular cartilage and to explore the function of cartilage injury–related lncRNAs (lncRNACIR) in OA.

Materials and Methods:
To identify lncRNAs specifically expressed in OA cartilage, we compared the expression of lncRNAs in OA cartilage with that in normal cartilage using microarray and quantitative polymerase chain reaction (qPCR) analyses. In OA cartilage, lncRNA-CIR was specifically, differentially, and highly expressed. The function of lncRNA-CIR was determined by silencing and overexpression in vitro. Extracellular matrix (ECM)–related molecules were detected by PCR, Western blot, and immunofluorescence analyses.

Results:
Up to 152 lncRNAs were found to be differentially expressed (>8-fold) in OA and normal cartilage (82 lncRNAs more highly expressed and 70 less highly expressed in OA cartilage than in normal cartilage). A specific differentially expressed lncRNACIR was selected according to the results of the higher expression in OA cartilage and OA chondrocytes. The expression of lncRNA-CIR increased in chondrocytes with in vitro treatment with interleukin-1 and tumor necrosis factor. Silencing of lncRNA-CIR by small interfering RNA promoted the formation of collagen and aggrecan and reduced the expression of matrixdegrading enzymes, such as MMP13 and ADAMTS5. The expression of collagen and aggrecan was reduced, whereas the expression of matrix-degrading enzymes was increased, after overexpression of lncRNA-CIR.

Discussion:
Our data indicate that 152 lncRNAs were either overexpressed or underexpressed in OA. It has been suggested that the observed changes have a biologic effect, and lncRNAs are not simply nonfunctional elements, but instead, they are key regulators of gene expression. The mechanism needs to be confirmed by further specific studies. Deciphering the precise molecular mechanisms of lncRNA function in OA will be critical to understanding the pathogenesis of OA and exploring new potential targets for therapy.

Conclusion:
The results indicate that lncRNACIR contributes to ECM degradation and plays a key role in the pathogenesis of OA. We propose that lncRNA-CIR could be used as a potential target in OA therapy.
References: