读书报告

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Role of autophagy in the progression of osteoarthritis:The autophagy inhibito76 r, 3-methyladenine, aggravates the severity of experimental osteoarthritis

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Role of autophagy in the progression of osteoarthritis: The autophagy inhibitor, 3-methyladenine, aggravates the severity of experimental osteoarthritis

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abstract

1、For this purpose, a cellular model of OA was generated by stimulating SW1353 cells with interleukin (IL)-1β and a rabbit model of OA was also established by an intra-articular injection of collagenase, followed by treatment with the autophagy specifc inhibitor, 3-methyladenine (3-MA).

2、Cell viability was analyzed by MTS assay, and the mRNA expression levels of matrix metalloproteinases (MMP)-13 and tissue inhibitor of metalloproteinase (TIMP)-1 were determined by RT-qPCR. Cartilage degeneration was examined under a light microscope, and autophagosome and chondrocyte degeneration was observed by transmission electron microscopy.

INTRODUCTION

1、The death of chondrocytes is a hallmark of cartilage degeneration in OA; however, the mechanisms responsible for chondrocyte death in OA-affected cartilage remain largely unknown. Autophagy plays a crucial role in maintaining cellular metabolism and homeostasis. However, excessive autophagy may lead to cell death. Autophagy is regulated by a series of autophagy-related genes (ATGs), such as Beclin-1 and light chain 3 (LC3). The expression levels of these genes are commonly used to monitor autophagic activity and flux.

2、A variety of cytokines, growth factors and enzymes, such as interleukin (IL)-1β and collagenase are involved in articular cartilage degeneration. Collagenase is upregulated in OA-affected cartilage and animal models of OA have been successfully established by an intra-articular injection of collagenase.

1、Cell viability.

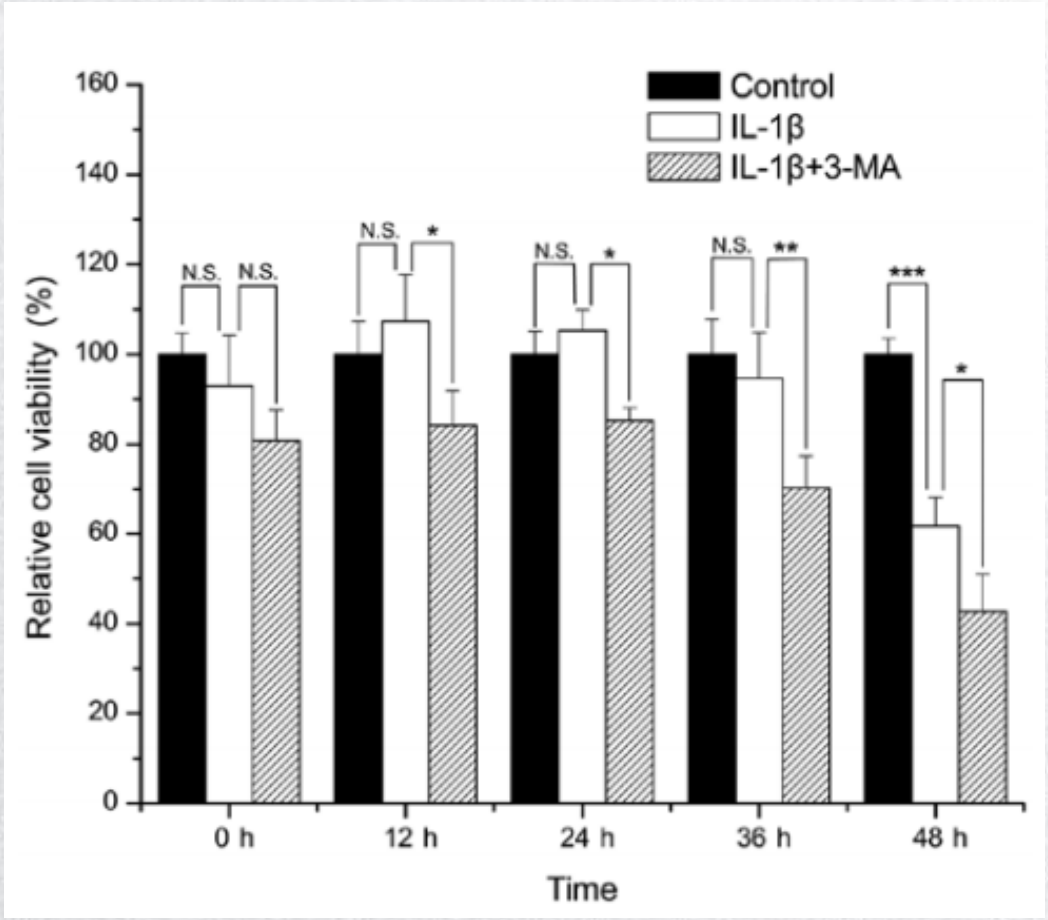


Figure 1. Comparison of the cell viability in interleukin (IL)-1β-stimulated SW1353 cells between the control and 3-methyladenine (3-MA)-treated cells. *P<0.05, **P<0.01, ***P<0.001. N.S., not signifcant.

2、Expression of MMP-13 and TIMP-1.

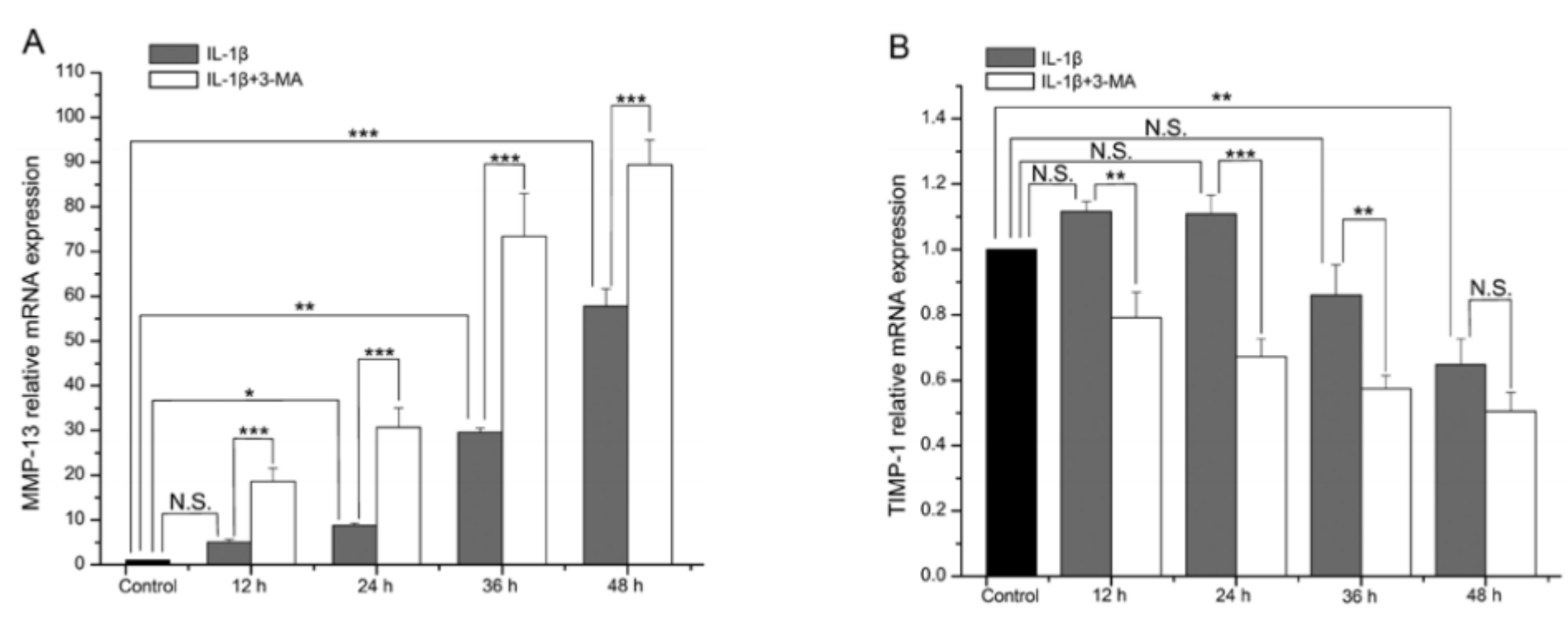
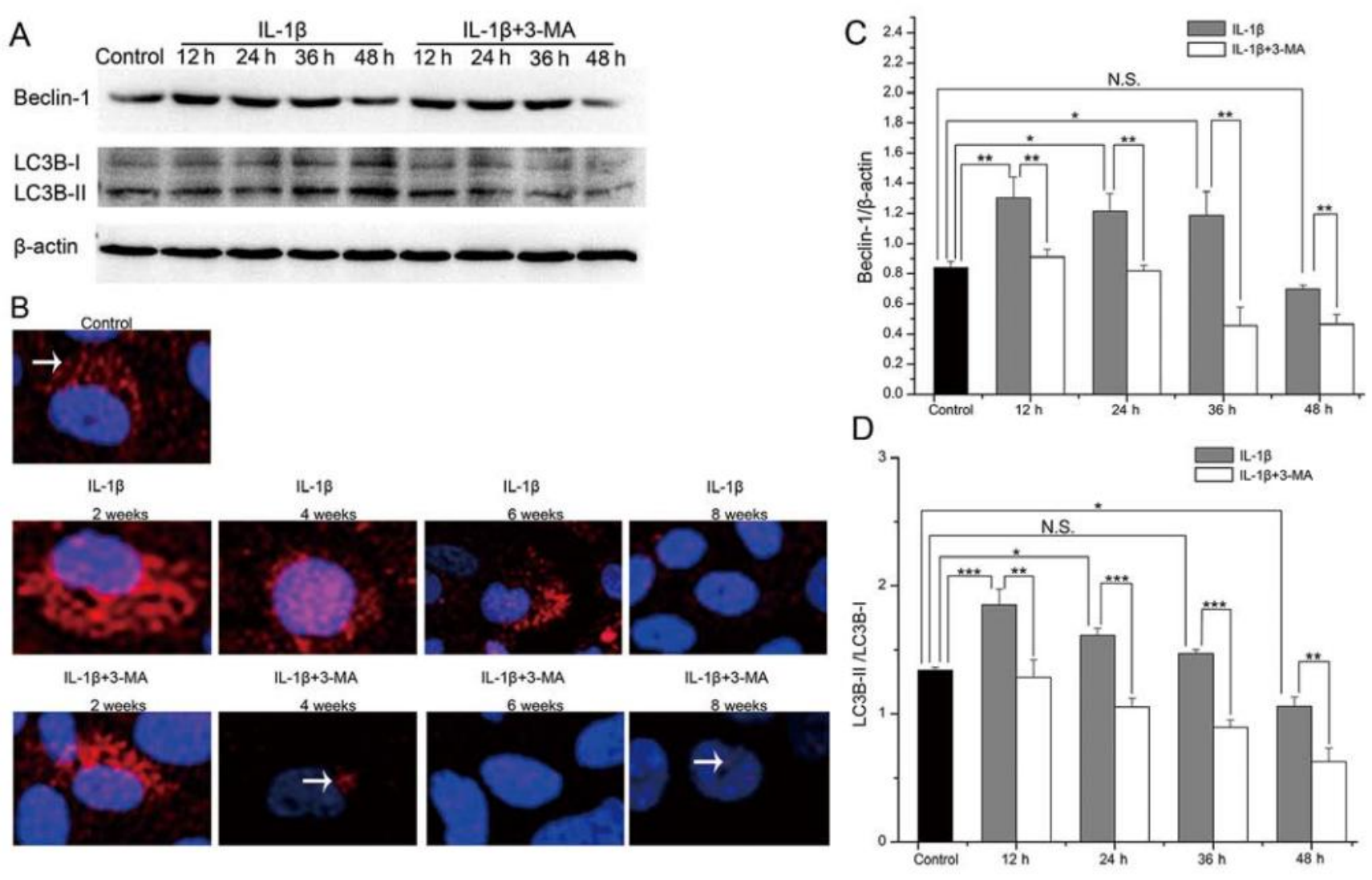
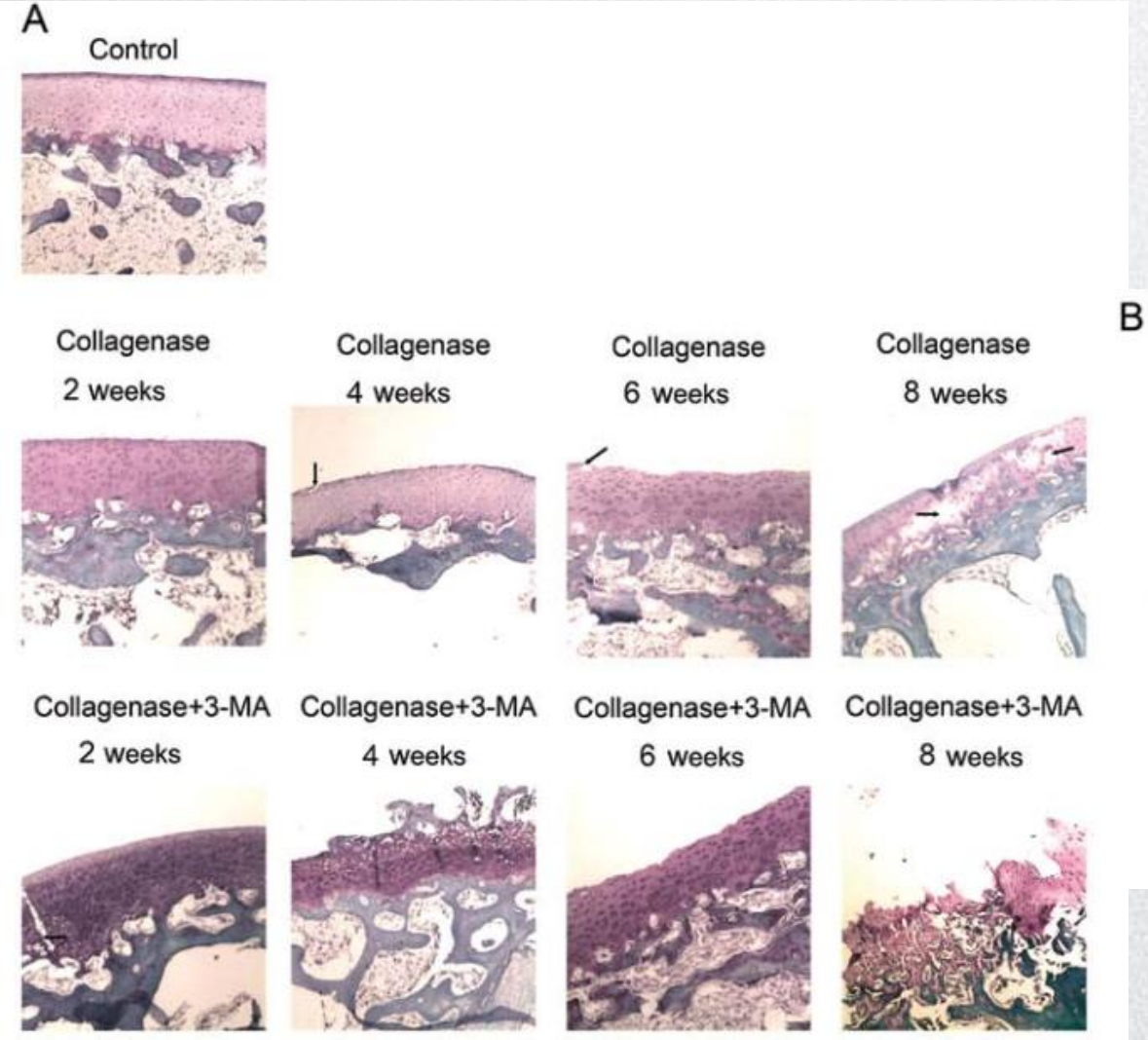


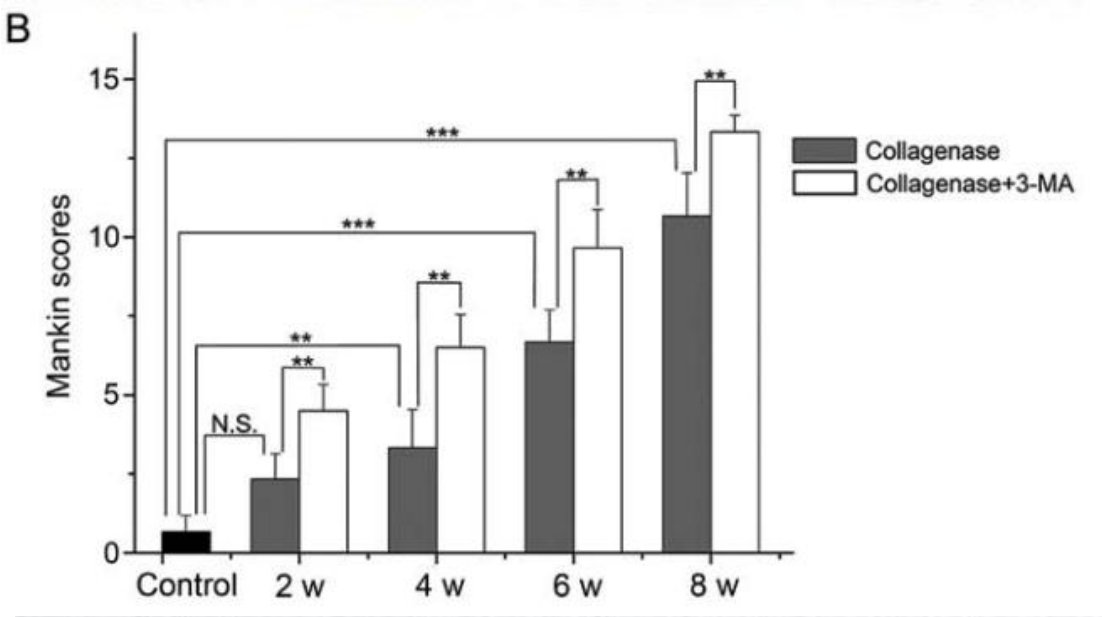
Figure 2. (A) Comparison of the mRNA expression level of matrix metalloproteinase (MMP)-13 in interleukin (IL)-1β-stimulated SW1353 cells between the control and 3-methyladenine (3-MA)-treated cells. (B) Comparison of the mRNA expression level of tissue inhibitor of metalloproteinase (TIMP)-1. *P<0.05, **P<0.01, ***P<0.001. N.S., not signifcant.

3、Expression of Beclin-1 and LC3B in IL-1β-stimulated SW1353 cells.

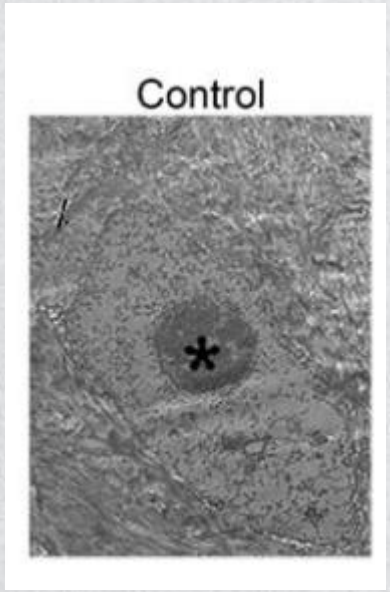


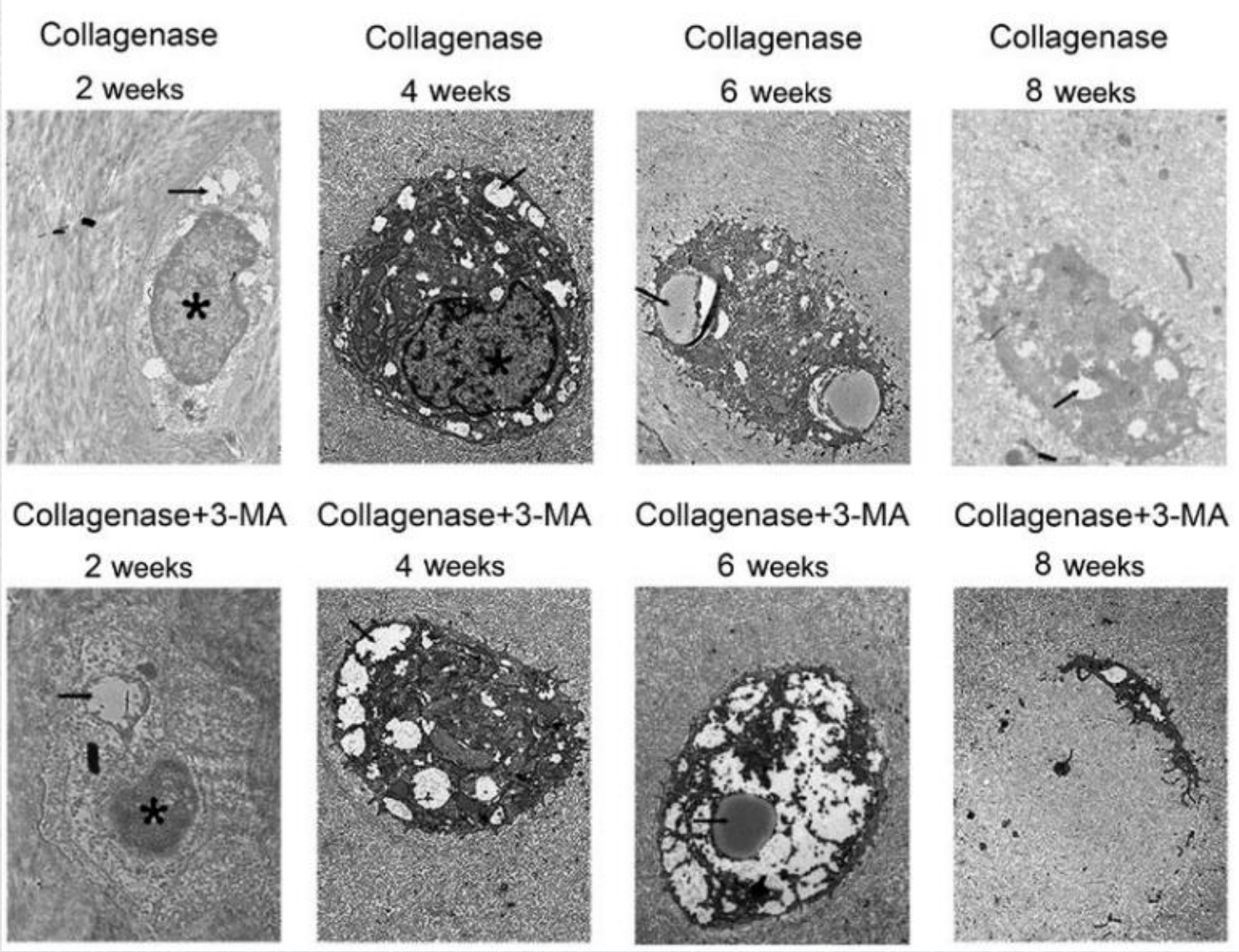
4、Histological evaluation.



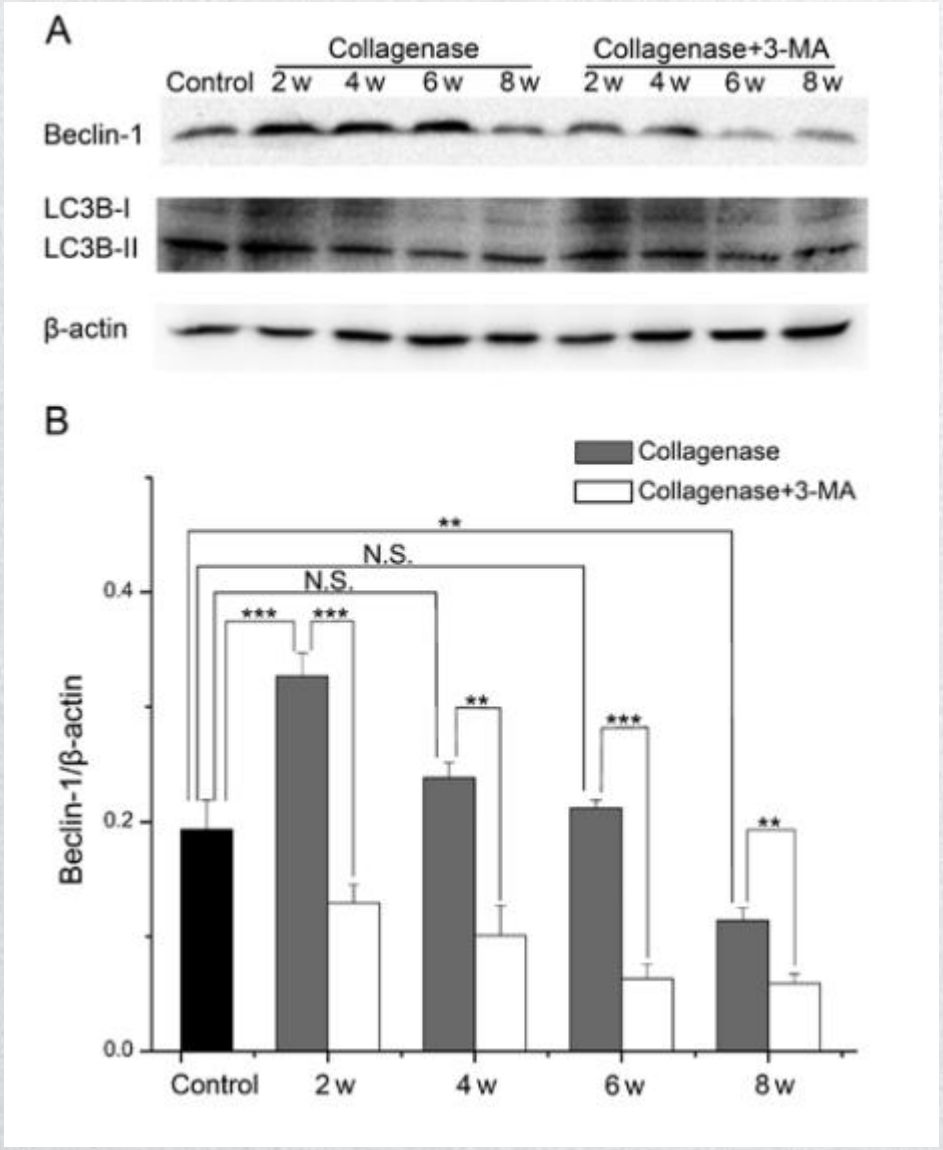


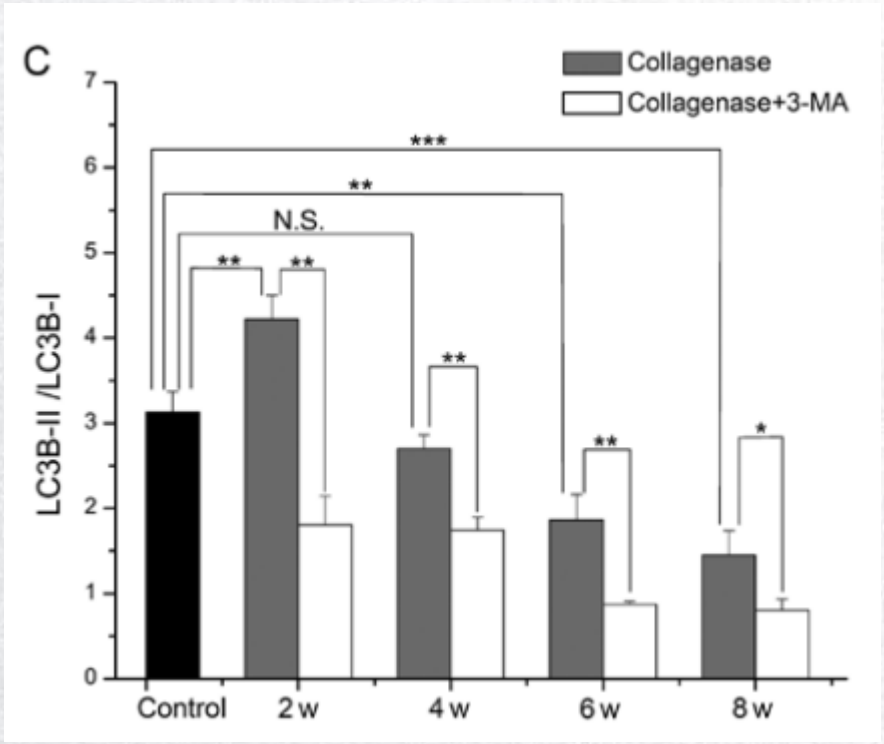
5、Transmission electron microscopy.





6、Expression of Beclin-1 and LC3B in cartilage from rabbit with OA.





Discussion

1、IL-1β stimulates the expression of collagenase in chondrocytes and is often applied to produce cellular OA models for *in vitro* studies, and a number of of studies have shown that SW1353 cells can take the place of human chondrocytes for research .

2、Recent studies have demonstrated that autophagy is involved in certain bone and cartilage diseases, such as cervical disc degeneration, cartilage degeneration of the temporomandibular joint , degradation of Meckel's cartilage and OA . However, the results regarding changes in autophagy and the specifc role of autophagy in the progression of OA are sometimes contradictory.

3、Autophagy was frst enhanced and then weakened in IL-1β-stimulated SW1353 cells and in rabbits with collagenase-induced OA degenerative cartilage. 3-MA aggravated the severity of experimental OA via the inhibition of autophagy, suggesting that the regulation of autophagy may be a potential therapeutic strategy for the treatment of OA.

THANKS

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