B-cell-specific mammalian target of rapamycin complex 1 activation results in severe osteoarthritis in mice

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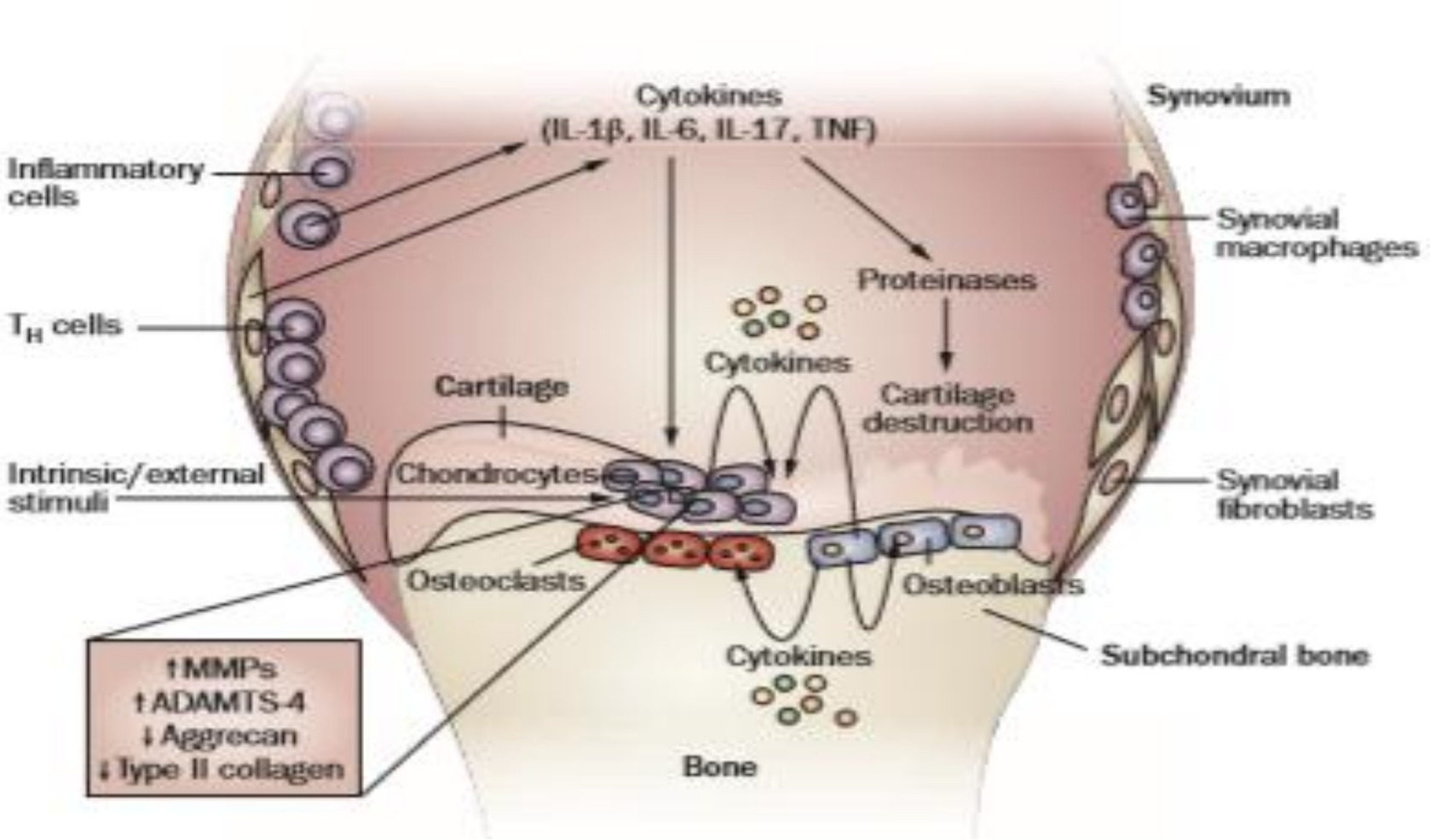
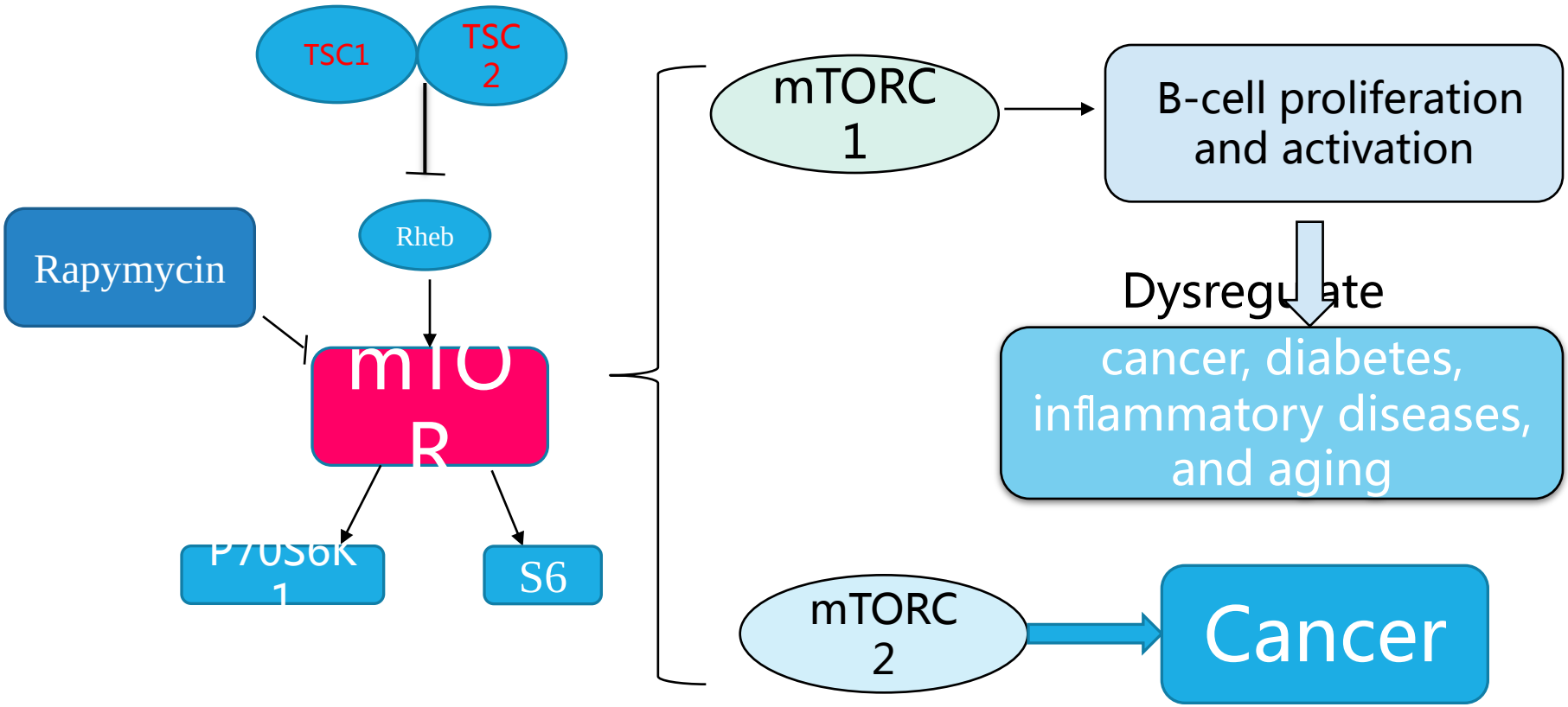
Introduction



INTRODUCTION

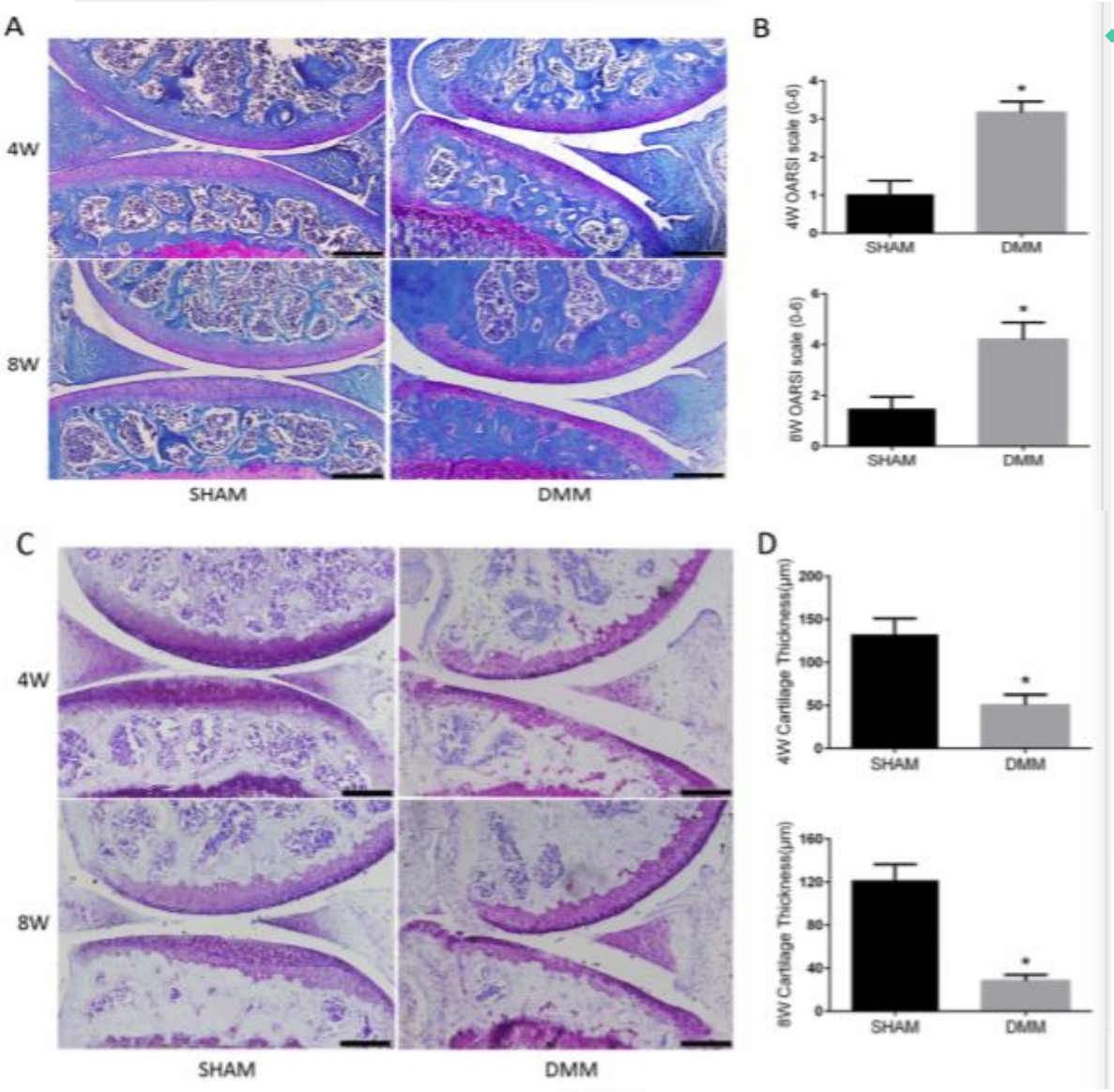


Materials and Methods

- 1.KO mice(CD19-Cre and TSC1flox/flox mice)
- 2. OA model（DMM)
- 3.B-Cells isolation
- 4. qPCR
- 5.Western blotting
- 6. Enzyme-linked immunosorbent assay（ELISA ）
- 7.Immunohistochemistry

Results：

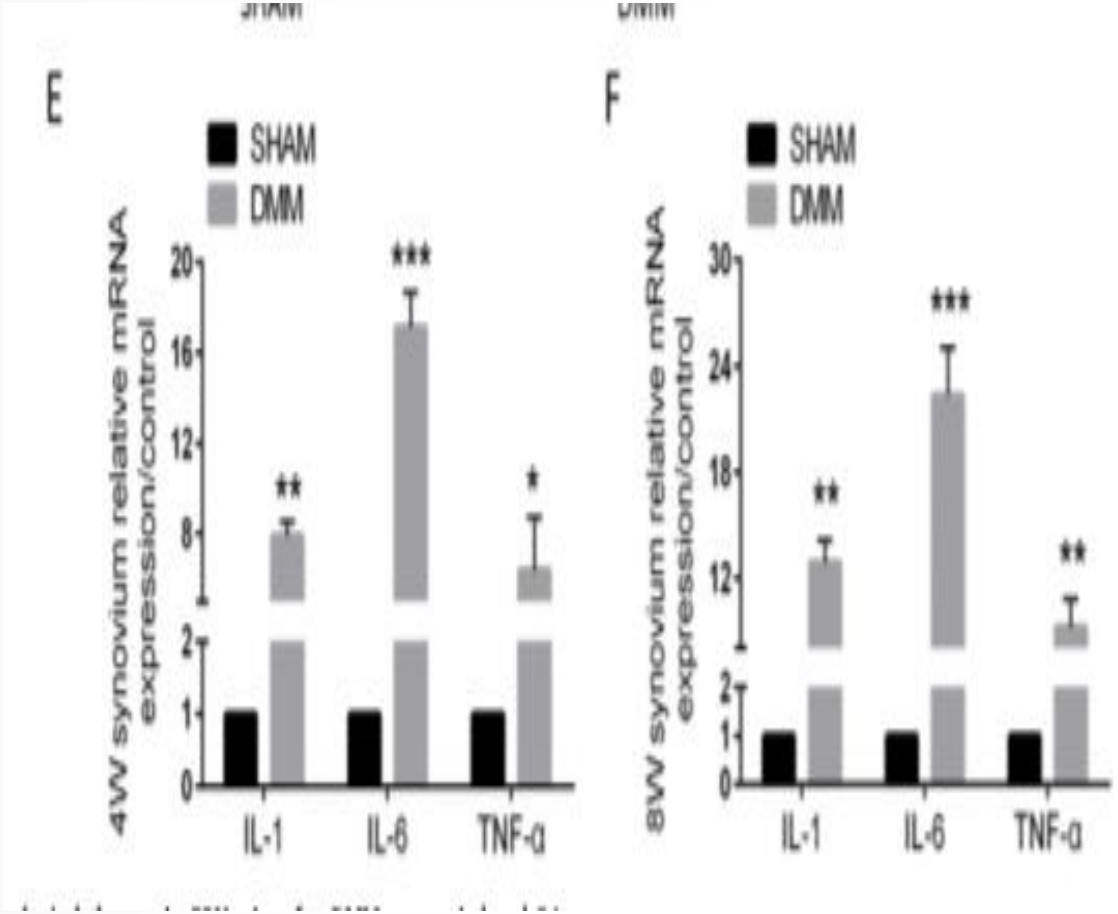
1. Histological changes in CON mice after surgically induced OA



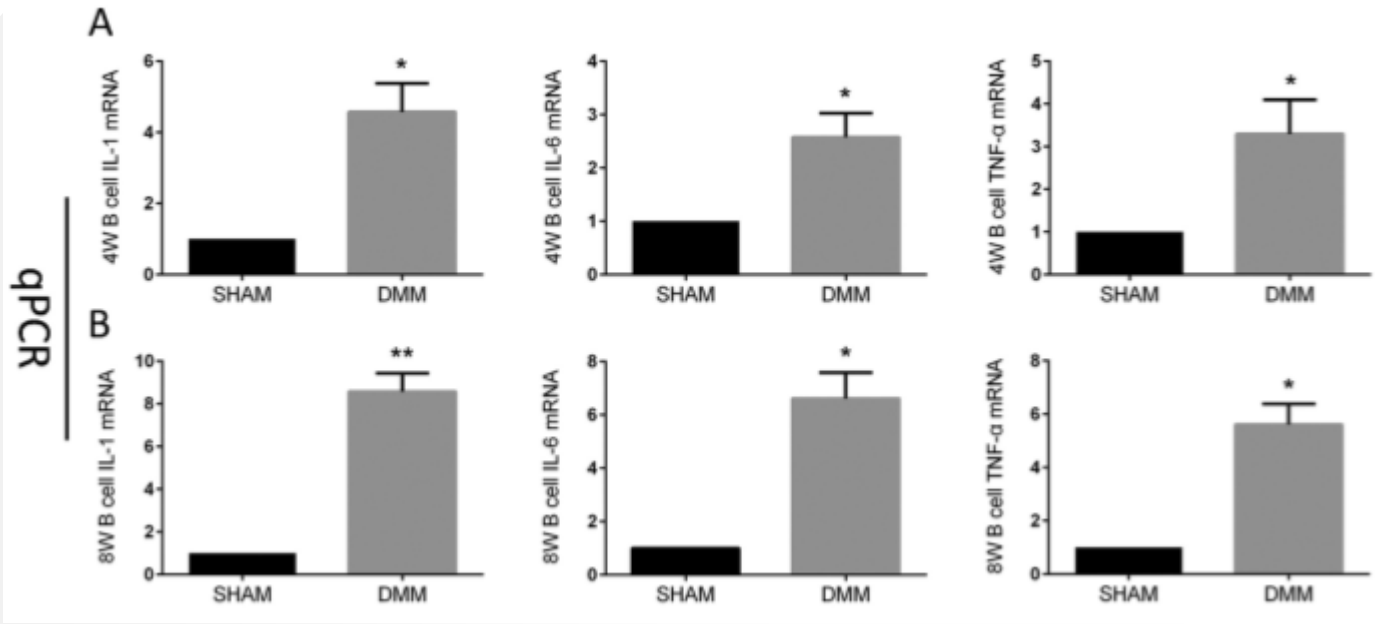
- The OARSI score was significantly increased in DMM group compared with SHAM .Joint cartilage thickness, assessed by toluidine blue staining,showed severe abrasion and significantly reduced cartilage thickness in the DMM compared with the SHAM group at 4 and 8weeks after surgery.

1.Histological changes in CON mice after surgically induced OA

Gene expression levels of the inflammatory cytokines IL-1β, IL-6, and TNF-α in the synovial membrane at 4 and 8weeks after surgery showed similar trends, as assessed by qPCR, with significantly higher levels in the DMM group compared with the SHAM group).



2. Inflammatory cytokine changes in serum and B cells in CON mice after surgically induced OA



Gene expression levels of inflammatory cytokines in B cells measured by qPCR were also significantly higher at 4 and 8weeks after surgery in the DMM compared with the SHAM group gene expression levels of inflammatory cytokines in B cells measured by qPCR were also significantly higher at 4 and 8weeks after surgery in the DMM compared with the SHAM group.

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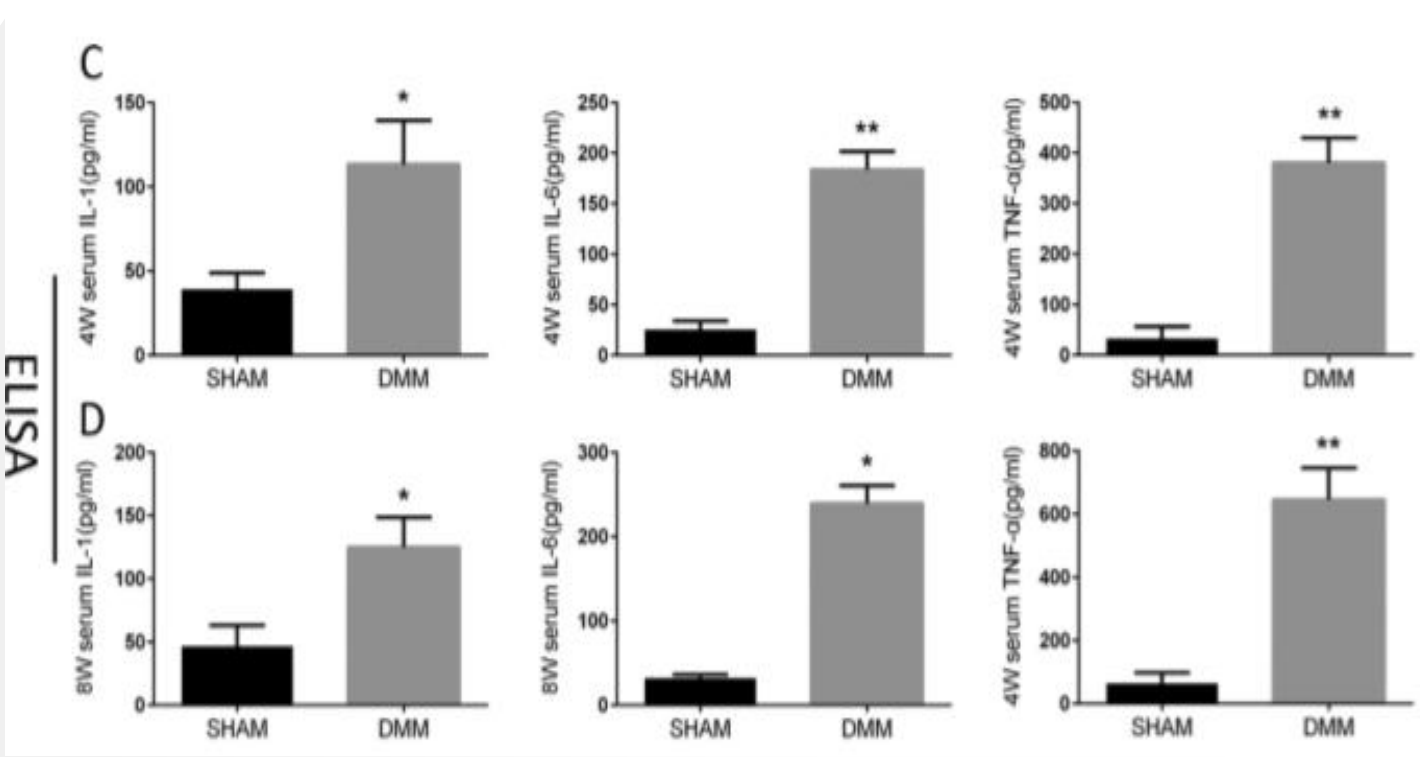
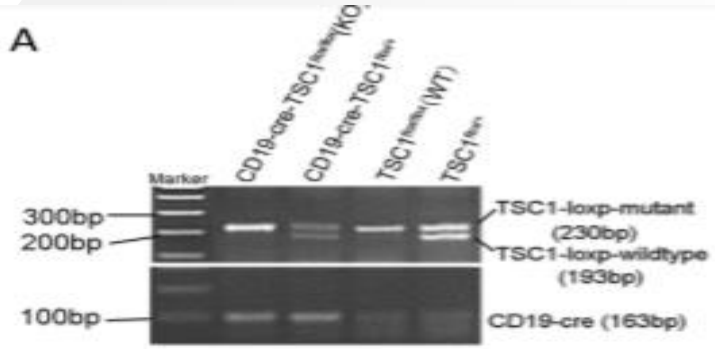
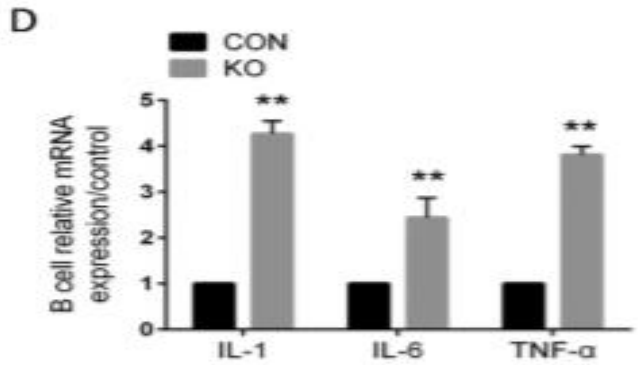
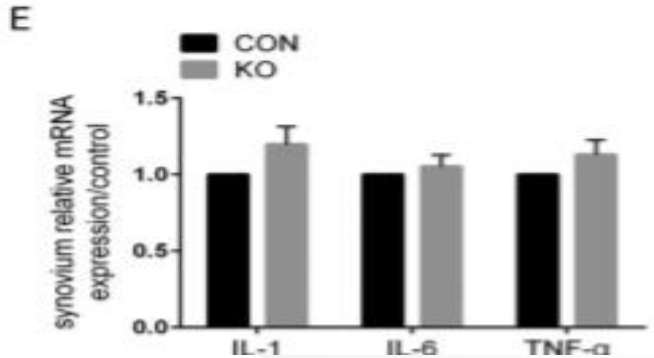


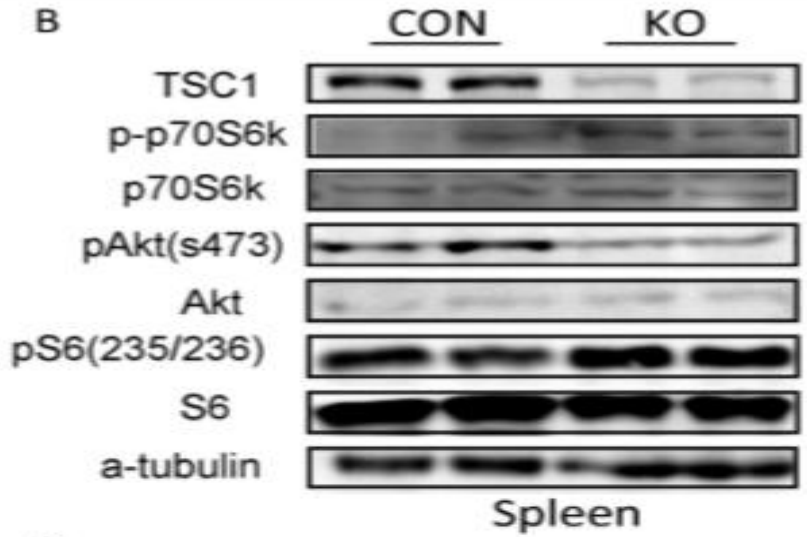
Serum IL-1β, IL-6, and TNFα protein levels were significantly higher in the DMM group at 4 and 8weeks.

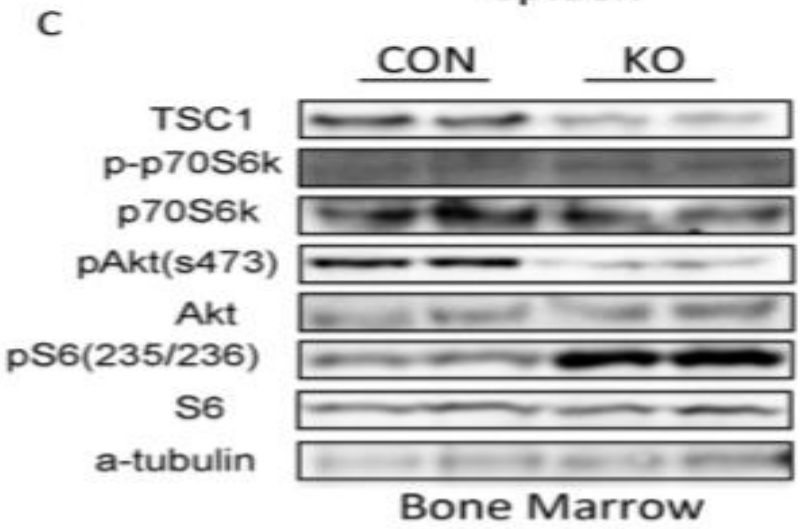
3. Differences in expression of inflammatory cytokines between KO and CON mice



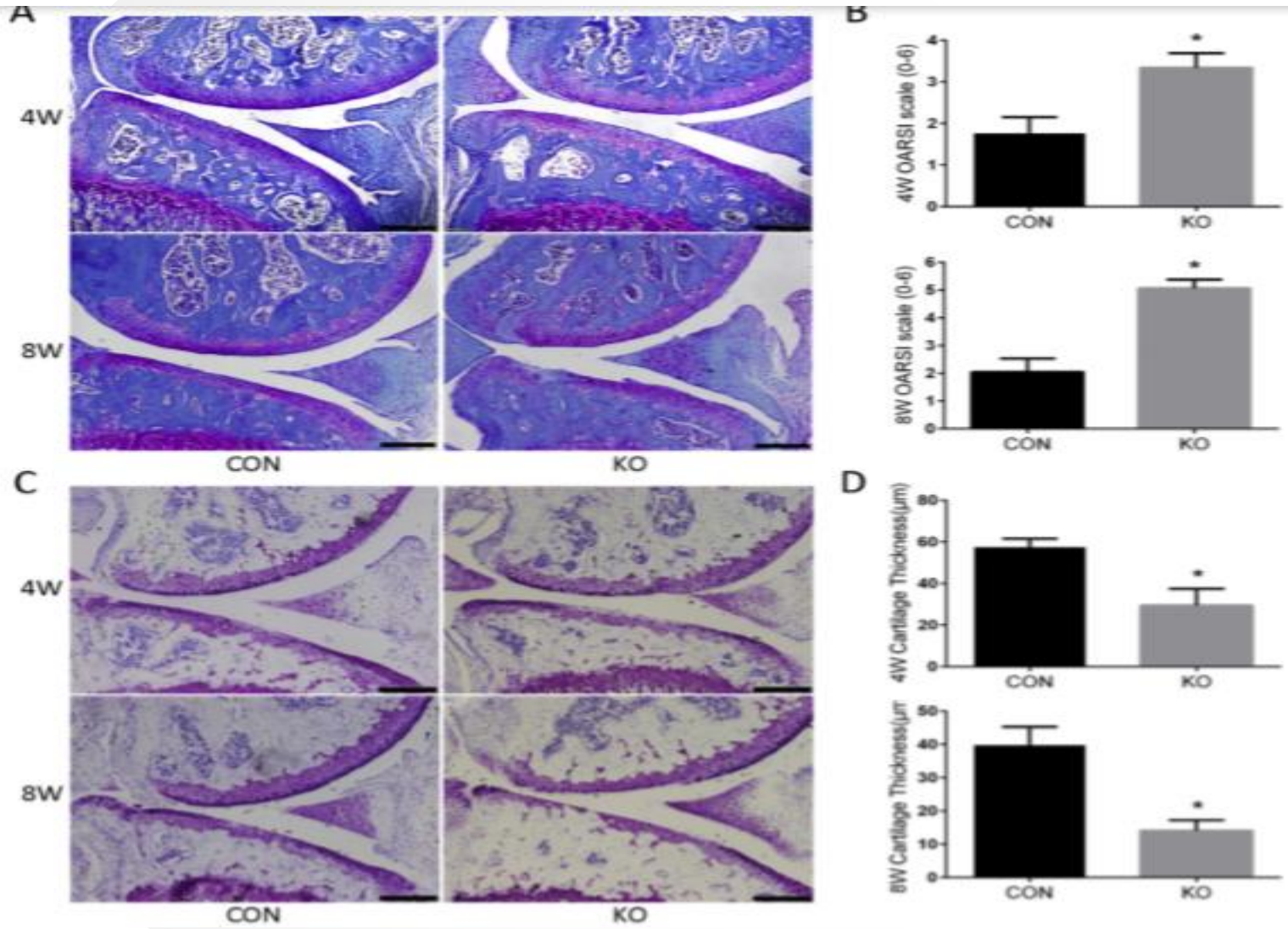








4. KO mice exhibited accelerated OA phenotype



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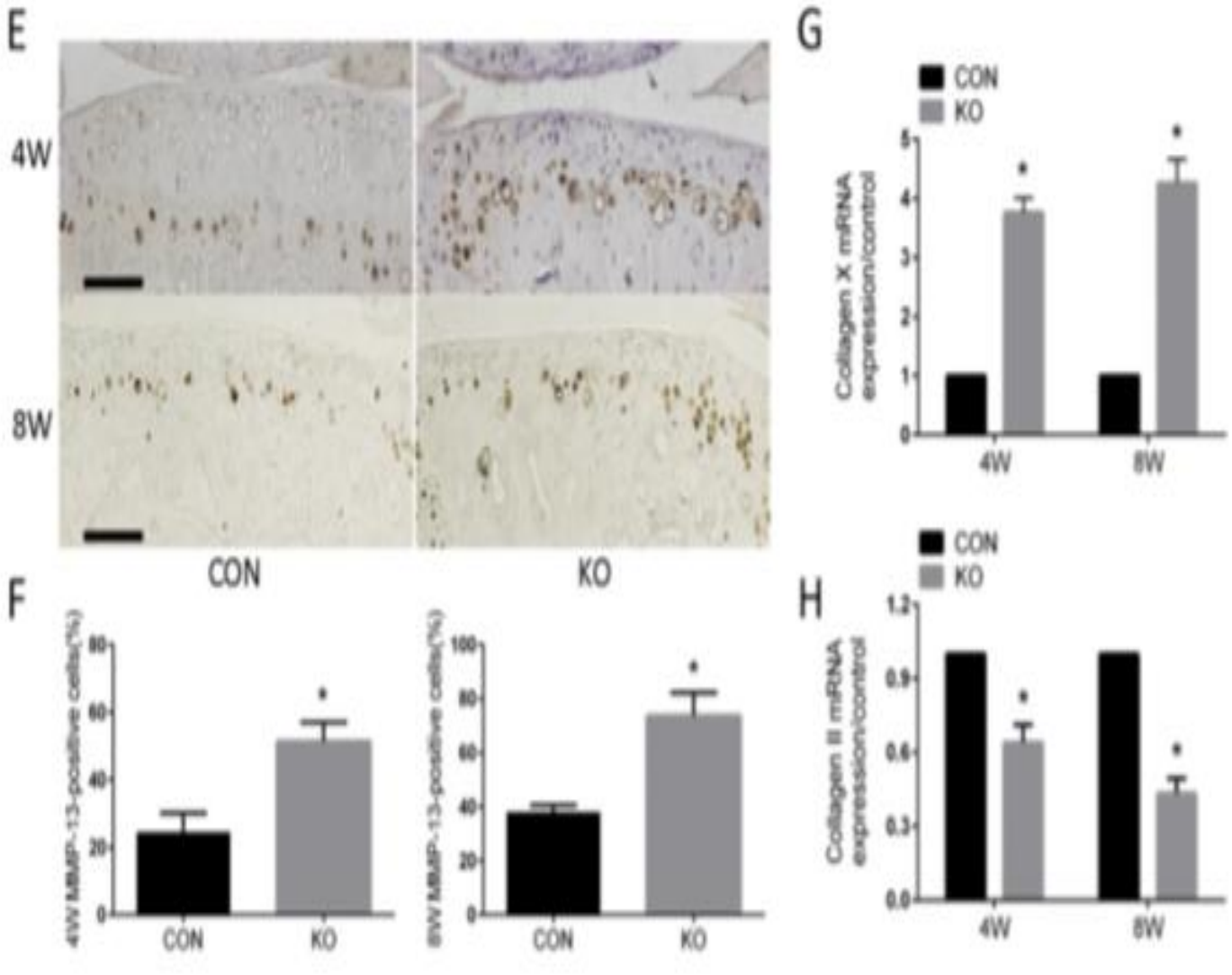
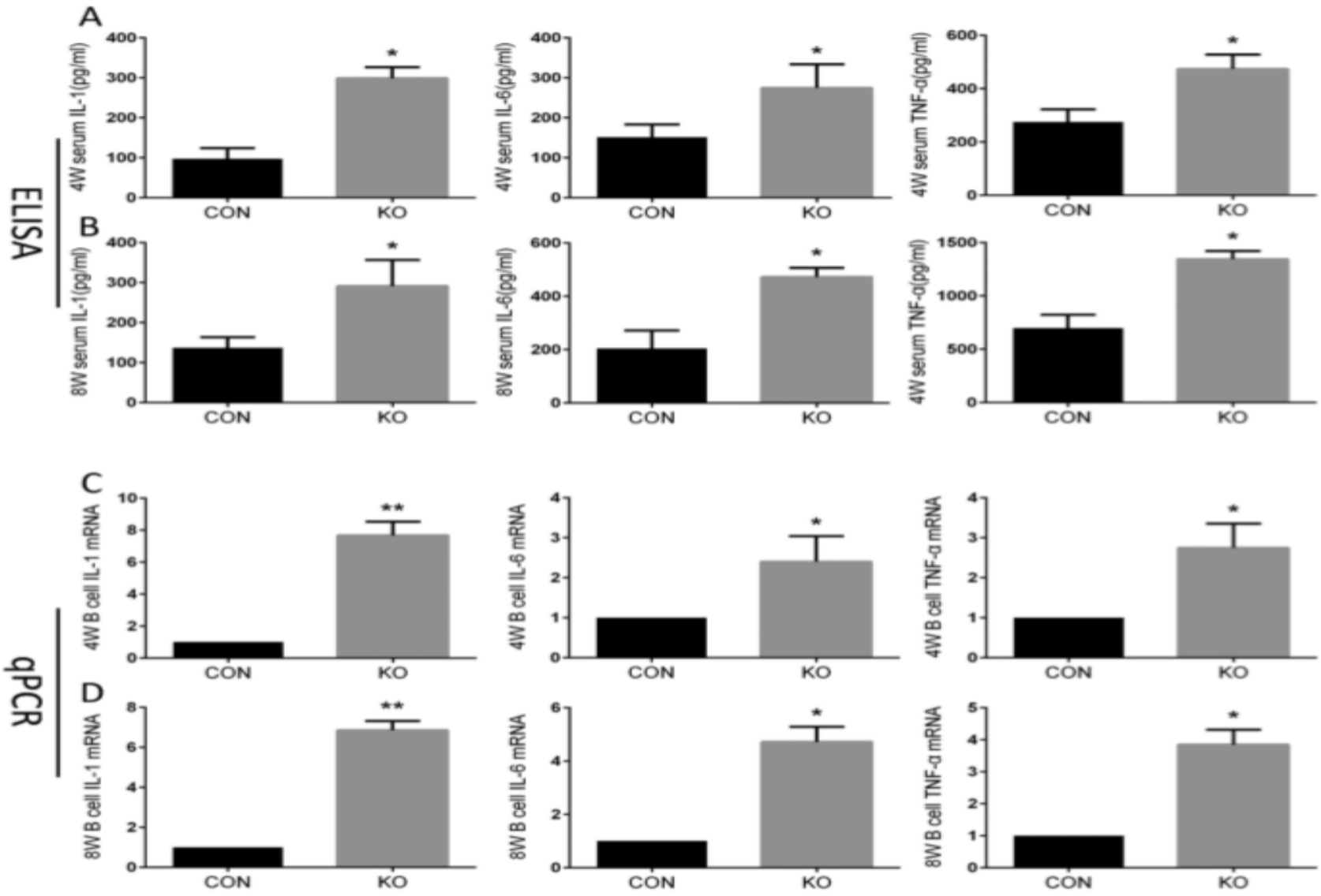


5. KO mice exhibited more severe inflammatory response after surgically induced OA



Discussion

- These results suggest that increased synthesis of inflammatory cytokines by B cells in KO mice may aggravate synovial membrane inflammation and cartilage destruction, thereby accelerating the progression of OA.

Conclusions

- This study demonstrated that activation of mTORC1 in B cells is associated with more severe OA.

Thank you for your attention!