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The complement regulator CTRP6 can suppress the development of collagen-induced arthritis in mice

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Abstract

Rheumatoid arthritis (RA) is a systemic, chronic and inflammatory disorder, mainly affecting joints and the pathogenesis has not been completely elucidated. We have already established two RA model mice; HTLV-I transgenic (Tg) mice and IL-1 receptor antagonist-deficient (KO) mice. C1qtnf6 is highly expressed in both RA model mice. In addition, C1QTNF6 locus is one of susceptibility loci for RA. C1qtnf6 encodes CTRP6 (C1qTNF-related protein 6), is a member of CTRP family that possesses complement C1q domain. It is reported that complement activation is important for the pathogenesis of RA. Thus, CTRP6 may be involved in RA pathogenesis. To elucidate the pathological role of CTRP6 in the development of arthritis, we have generated C1qtnf6 eficient (KO) and tansgenic (Tg) mice. Collagen-induced arthritis (CIA) was exacerbated in C1qtnf6KO mice due to enhanced complement activation. On the other hand, C1qtnf6 Tg mice were resistant to CIA. We found that CTRP6 suppressed the alternative pathway of the complement system by forming a complex with C3 and competing with factor B for the C3 binding. Furthermore, injection of recombinant CTRP6 to arthritis mice could ameliorate the arthritis. These observations indicate that CTRP6 is an endogenous regulator of the complement alternative pathway and could be a good medicine for the treatment of rheumatoid arthritis in humans.