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IL-37b alleviates inflammation in the temporomandibular joint cartilage via IL-1R8 pathway

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Abstract

Objectives: Interleukin (IL)-37 is a natural suppressor of innate inflammation. This study was conducted to explore the anti-inflammatory effects of IL-37 in temporomandibular joint (TMJ) inflammation.

Materials and Methods: The expression of IL-37 in the TMJ was measured using ELISA and IHC. Human TMJ chondrocytes were treated with IL-37b and IL-1β, and inflammation-related factors were detected. siRNA-IL-1R8 was transfected into chondrocytes, and the affected pathways were detected. IL-37b was used in disc-perforation-induced TMJ inflammation in SD rats. Micro-CT, IHC, real-time PCR and histological staining were used to quantify the therapeutic effect of IL-37b.

Results: IL-37 was expressed in the synovium and the disc of patients with osteoarthritis (OA) and in the articular cartilage of condylar fracture patients. IL-37 was highly expressed in synovial fluid of patients with synovitis than in those with OA and disc displacement and was closely related to visual analogue scale (VAS) score. In vitro, IL-37b suppressed the expression of pro-inflammatory factors. In addition, IL-37b exerted anti-inflammatory effects via IL-1R8 by inhibiting the p38, ERK, JNK and NF-κB activation, while silencing IL-1R8 led to inflammation and upregulation of these signals. In disc-perforation-induced TMJ inflammation in SD rats, IL-37b suppressed inflammation and inhibited osteoclast formation to protect against TMJ.

Conclusions: IL-37b may be a novel therapeutic agent for TMJ inflammation.

1 | INTRODUCTION

The temporomandibular joint (TMJ) is a synovial joint that is frequently affected by osteoarthritis.[1] Temporomandibular joint osteoarthritis (TMJOA), which is considered a prevalent chronic pain disease, leads to cartilage degeneration, subchondral bone remodelling and synovitis, thus influencing biopsychosocial conditions.[2,3] Inflammation is believed to be the chief cause of pain in patients with OA, resulting from the release of pro-inflammatory cytokines.[4] Increasing evidence indicates that inflammation plays a critical role in the pathogenesis of TMJOA.[5,6] Condition of TMJ disc displacement without restoration (DDWoR) is mainly characterized by mouth-opening limitations.[7] TMJ synovitis, the most common early-detected inflammatory arthritis, always causes joint pain, especially during acute inflammation.[8] IL-1β is the major pro-inflammatory cytokine that exhibits destructive effects that are characterized by increasing cartilage degradation and suppression of cartilage matrix synthesis.[9-11] Excess production of

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