

## **New insights into the treatment of joint destruction in rheumatoid arthritis by traditional Chinese medicine based on novel technologies**

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### **Abstract:**

Rheumatoid arthritis (RA) is a prototypic autoimmune diseases affecting joints. The characteristic pathological lesions are inflammation and destruction of bone and cartilage in affected joints. Medical drug treatment is currently the main avenue of RA therapy. As the regulation of different and multiple related therapeutic targets by Traditional Chinese medicines (TCMs) and their active ingredients were associated with greater therapeutic benefits, TCMs are precious resources for finding novel agents for treating joint destruction of RA. Newly generated knowledge from advanced modern technologies such as next-generation sequencing (NGS), single-cell sequencing (scRNA-seq) and an intravital imaging system using two-photon microscopy has contributed to elucidate the transcriptomics and dynamics of specific cells involved in pathological osteoclastogenesis with the treatment of TCMs, improving our understand of TCMs action for the pathophysiology of inflammatory and autoimmune osteolytic diseases. The NGS has provided important insights into the finding of key effector cells in the treatment of TCMs through characterizing individual cells in the synovial microenvironment. The application of scRNA-seq to the cellular heterogeneity within a biological system enabled the identification of specific subpopulation differentiating into pathological mature osteoclasts within the previously defined 'osteoclast precursor-containing population'. In addition, an intravital imaging technology using two-photon microscopy has been applied to the synovial tissues of arthritic mice to observe the real-time dynamics of osteoclasts and immune cells in the bone marrow. Future technologies, such as high resolution spatial transcriptomics, will enable step changes integrating single cell transcriptomic and geographic data to provide an integrated understanding of pathology in joints. All these advanced modern technologies are intended to provide comprehensive information and reference for exploring new therapeutic strategies of TCMs in the RA treatment. Here, we review and discuss how novel technologies help to better

understand the pathogenesis of bone erosion and unravel the complexities and in-depth mechanisms of TCMs in alleviating RA bone destruction, especially the phenotypic and molecular characteristics of resident macrophages, fibroblasts, osteoclast and highlights their crosstalk during joint homeostasis and joint inflammation before and after treatment of TCMs, and provide some directions for the future development of TCMs as anti-RA drugs in clinical.

**Keywords:** Bone erosion; Novel technologies; Osteoclasts; Traditional Chinese Medicine

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