A cocktail of UC-MSCs and SB alleviated RA via ICOS/ICOSL

Abstract

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by progressive joint injury, cartilage and bone destruction, lung disease, vasculitis, neuropathy and other systemic tissue damage. Its pathogenesis is complex and has not yet been fully understood. Human umbilical cord derived mesenchymal stem cells (UC-MSCs) are multipotent stem cells from neonatal umbilical cord. Studies have found that UC-MSCs have a good therapeutic effect on autoimmune diseases such as systemic lupus erythematosus and RA. However, there are still some patients with UC-MSCs who are not effective in clinical treatment. In our study, PBMCs from RA patients were co-cultured with UC-MSCs. Our results showed that for RA patients with high expression of ICOS, UC-MSCs had a poor regulation effect on Tfh cells. We found that this may be related to the high expression of ICOS ligand (ICOSL) on UC-MSCs. Once ICOS/ICOSL is combined, the PI3K-AKT-mTOR pathway is activated, which triggers the subsequent inflammatory cascade reaction. Our results also found that silybin (SB) can directly bind to ICOS, suggesting that SB may bind to ICOS by competing with ICOSL on UC-MSCs, thereby inhibiting the activation of P pathway and reducing inflammation, and finally improving the anti-RA effect of UC-MSCs. treatment effect, finding a better method for UC-MSCs in the treatment of autoimmune diseases.

Key word: rheumatoid arthritis; UC-MSCs; silybin; ICOS/ICOSL