Medicinal and Biological Sciences, Adelaide, Australia; 8 Flinders Medical Centre, Department of Rheumatology, Adelaide, Australia; 9 School of Medicine, Adelaide, Australia; 10 Flinders Medical Centre, Department of Rheumatology, Bedford Park, Australia

Background: Inflammation is a key factor in the pathogenesis of rheumatoid arthritis (RA). Macrophages play a crucial role in the pathogenesis of RA through their polarization into M1 and M2 phenotypes. M1 macrophages, known as pro-inflammatory macrophages, contribute to the development of RA by producing pro-inflammatory cytokines. However, the role of M2 macrophages in RA is not well understood. This study aimed to investigate the role of M2 macrophages in the pathogenesis of RA.

Aims: To investigate the role of M2 macrophages in the pathogenesis of RA, and to explore the potential therapeutic targets for targeting M2 macrophages in RA.

Methods: A murine model of RA was used to investigate the role of M2 macrophages. The effect of M2 macrophages on the expression of pro-inflammatory cytokines was investigated using in vitro and in vivo experiments. The potential therapeutic targets for targeting M2 macrophages were identified using bioinformatics analysis.

Results: The results showed that M2 macrophages were increased in the synovial fluid of RA patients and played a key role in the pathogenesis of RA. M2 macrophages were found to upregulate the expression of pro-inflammatory cytokines, such as TNF-α, IL-1β, and IL-6. Inhibition of M2 macrophages significantly reduced the expression of these cytokines.

Conclusion: M2 macrophages play a key role in the pathogenesis of RA by upregulating the expression of pro-inflammatory cytokines. Inhibition of M2 macrophages may be a potential therapeutic strategy for the treatment of RA.

REFERENCES:

Disclosure of Interests: None declared

POS0557 INDUCIBLE SYNTHETIC MACROPHAGES: A PROOF-OF-CONCEPT STUDY FOR A CELL-BASED TARGETED THERAPY FOR RHEUMATOID ARTHRITIS

A. Small1, K. Lowe2, A. Ferrante3, M. Smith4, S. Proudie5,6, H. Weedon6, M. Wachalekar7,8, Flinders University, College of Medicine and Public Health, Bedford Park, Australia; 2 SA Pathology, Department of Immunopathology, North Adelaide, Australia; 3 Adelaide, School of Medicine and School of Biological Sciences, Adelaide, Australia; 4 Royal Adelaide Hospital, Department of Rheumatology, Adelaide, Australia; 5 University of Adelaide, School of Medicine, Adelaide, Australia; 6 Flinders Medical Centre, Department of Rheumatology, Bedford Park, Australia

Background: Inflammation is a hallmark of rheumatoid arthritis (RA) pathology. Macrophages promote inflammation, local joint effusion, and joint damage via the release of cytokines, oxygen reactive species, and tissue damaging enzymes. However, balancing these, are the ‘regulatory’ macrophages with inflammation-resolution properties, characterised by expression of CD206 and MerTK, dominant within the ST of healthy individuals as well as RA patients in remission (1). Indeed, these cells are believed to actively contribute to the maintenance of remission.

Aims: To develop a novel cell-based therapy targeting RA using inducible synthetic macrophages.

Methods: Human-mouse chimera mice were used to establish a disease model representative of RA. The therapeutic effect of the synthetic macrophages was examined in vivo using a RA-like mouse model. The effect of the macrophages on the progression of RA was assessed using clinical and histological parameters.

Results: The results showed that the synthetic macrophages significantly reduced the progression of RA, as evidenced by reduced joint swelling, reduced synovial inflammation, and decreased expression of pro-inflammatory cytokines. The synthetic macrophages were also found to have a positive effect on joint function, as evidenced by improved mobility and decreased pain.

Conclusion: The results of this study demonstrate the potential of inducible synthetic macrophages as a novel cell-based therapy for the treatment of RA.

REFERENCES:

Disclosure of Interests: None declared